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COCAINE INSIGHTS 2

Cocaine: A spectrum of products

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Going Beyond Drug Seizures

Cocaine Insights

The cocaine market presents a clear threat at global level. Well-defined locations of production in South America and large consumer markets in the Americas and Europe lead to trafficking routes from a circumscribed origin to specific, even if far-flung, destinations. While some parts of the world play a crucial role as transit regions, the routes, modalities and networks employed by criminal actors continue to evolve, diversify and become more efficient. The increasingly globalized, interconnected, digitalized and technologically sophisticated nature of society, as well as a growing affluent demographic in some regions where cocaine use has traditionally been low, can potentially catalyse and accelerate the dynamism and expansion of the market.

The series Cocaine Insights, developed by UNODC in the framework of the CRIMJUST programme and in cooperation with partners and stakeholders at national, regional and international levels, delivers the latest knowledge and trends on issues related to cocaine markets in an accessible and informative format.

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Disclaimer

Comments on the report are welcome and can be sent to:
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Abbreviations

DEA	Drug Enforcement Administration (United States)
EMCDDA	European Monitoring Centre for Drugs and Drug Addiction
SIMCI	Sistema Integrado de Monitoreo de Cultivos Ilícitos
UNODC	United Nations Office on Drugs and Crime

Executive summary

In the context of an ongoing expansion of the global cocaine market, this report summarizes the current state of knowledge on *what* the cocaine consumer products are and *how* they are produced and consumed in different world regions. The report is based on available published evidence and on the knowledge gained through UNODC's monitoring activities in South American countries.

It offers insight into the spectrum of cocaine products in order to assist practitioners in drug supply and drug demand reduction, such as law enforcement agencies and healthcare providers, to tailor their response to production, trafficking and consumption of cocaine products.

Knowledge gaps still remain in many world markets regarding the cocaine products available to users, in terms of their chemical form, purity, cutting agents used for dilution and adulteration, price and routes of administration.

Cocaine is consumed worldwide in a base or a salt form

Cocaine, an alkaloid extracted from the leaves of two species of coca plant, is found worldwide in a variety of consumer products that come in two chemical forms, as a base and as hydrochloride salt. Nasal insufflation ("sniffing", "snorting") of cocaine in its salt form, and the inhalation of the vapours when cocaine in its base form is smoked, are the most frequently used routes of administration at global level, followed by injection and oral use.

Depending on the main ingredient and the method of manufacturing, it is possible to distinguish three main families of products derived from the base and salt forms:

(1) manufacturing process consumer products (MCPs) derived from coca paste and cocaine base;

(2) freebase consumer products (FCPs) derived by converting cocaine salt back to base form;

(3) consumer products based on cocaine hydrochloride (typically in powder form).

Manufacturing process consumer products (MCPs) popular in South America under different street names

MCPs, mostly smokable substances made from coca paste and/or cocaine base, are mainly found in South America. Street names for these products vary from country to country. Moreover, one name can refer to different products in different countries. A range of MCPs, most likely made from coca paste are referred to as *paco* (Argentina, Uruguay), *pitillo* (Bolivia), *merla* (Brazil), *mono* (Chile), *basuco* (Colombia and Venezuela, where it is sometimes adulterated with caffeine and phenacetin), *baserolo* (Ecuador), *pay* (Peru), *chespi* (Paraguay) among others. These products are typically smoked, both mixed with tobacco or marijuana, or pure using home-made pipes.

Some of the MCPs made of a solid form of cocaine base found on South American markets are referred to as "crack" by local consumers. However, this should be differentiated from the conventional term "crack" that refers to a product obtained from cocaine hydrochloride available in North American and European markets.

"South American Crack"

"Crack", a solid form of cocaine base, is especially popular in Brazil, while its variants are also found in Uruguay, Paraguay as well as in coca producing countries (Bolivia, Colombia and Peru). While products known as "crack" in South America may come in multiple forms, they typically differ from those found in North America and Europe, in that they appear to be predominantly obtained from cocaine in base form.

The so-called "South American crack" made in Bolivia, Colombia and Peru may be smuggled to other South American countries where it is received in 1-kilo bricks and retailed in the form of small rocks, but it is also possible that "crack" is manufactured in destination countries such as Brazil from dried coca paste and/or cocaine base trafficked from Andean countries and pressed into 1-kilo bricks.

Freebase and "crack" can both be obtained from cocaine hydrochloride, but "crack" is less pure, easier to make and more prevalent

The freebase consumer products (FCP) include "freebase" in addition to "crack" as found in the European and North American markets. Both of these primarily smokable products are prepared by transforming the cocaine hydrochloride salt into a base form that has been freed of hydrochloric acid. The key difference lies in the final stages of the process; making "freebase" involves an additional extraction step by means of an organic solvent to eliminate impurities, thus resulting in a purer form of cocaine than "crack." This method is dangerous because of the use of a highly flammable organic solvent, typically diethyl-ether, that can ignite if subjected to heat or a flame and may cause severe burns.

In contrast, "crack" is relatively easy and safe to manufacture at home from cocaine hydrochloride, which may explain its

popularity on many drug markets in Europe, the Americas and elsewhere. However, as little or no purification is involved in its preparation, "crack" usually contains most of the impurities, diluents and adulterants intrinsic to the starting material. The purity of the final product in both "crack" (as found on the European and North American markets) and "freebase" depends largely on the purity of the cocaine hydrochloride used as starting material.

Contents of cocaine hydrochloride products evolve constantly

Cocaine hydrochloride ("powder cocaine") is the salt most frequently encountered in cocaine consumer products. It comes in the form of powder containing varying amounts of other substances which can be categorized either as impurities (alkaloids, solvents, and cocaine base) or as cutting agents (diluents and adulterants). While impurities can constitute up to 10% of the total, cutting agents account by far for the largest proportion of the non-cocaine material found in most cocaine hydrochloride powders. They are usually added along the illicit distribution chain to increase product volume and profits. Unlike precursors and essential chemicals, cutting agents are typically not subject to international control, although some may be subject to controls under national health and/or food regulations.

Impurities and cutting agents come from three different sources: the plant material used to manufacture cocaine hydrochloride; the cocaine manufacturing process; and the process of dilution and adulteration. Combinations and concentrations change over time as illicit manufacturing processes evolve in response to changes in global cocaine market.

(Bi)carbonates and sugars, most popular diluents in South America and Europe respectively

Diluents are inert, pharmacologically inactive substances, many of which are routinely used in the food industry and can be purchased with relative ease at comparatively low prices. The available literature suggests that the cocaine diluents most frequently found in South America are carbonates and bicarbonates, whereas those most frequently used in Europe are sugars. The process of diluting cocaine hydrochloride is more likely to occur in transit and consumer countries than in producing countries.

Levamisole and phenacetin, most frequently found adulterants

Most of the adulterants found in cocaine hydrochloride powders are pharmaceutical drugs, and they tend to be more expensive and harder to procure than diluents since they may be subject to more national controls. Local anaesthetics appear to be the substances with the longest history of use as cocaine adulterants, while levamisole (a substance widely used in veterinary medicine) and phenacetin (an analgesic) appear as those most frequently found in the last 10 to 15 years. Many cocaine adulterants pose significant health risks as they amplify the toxicologic effects of cocaine. More rarely, adulterants are other illicit drugs like amphetamine and methamphetamine, and even more rarely they include new psychoactive substances.

Adulterants have diversified but cocaine purity has increased

The range of adulterants found in cocaine hydrochloride samples has increased since the 1980s, and especially since the early-2000s, in Europe and the Americas. However, there are indications that adulterant concentrations in cocaine powders have decreased recently both in source countries and in destination markets, while cocaine purity has increased. These developments reflect a greater availability of cocaine in the global cocaine market in the 2010s.

Policy implications

Despite the fact that cocaine is extracted from a natural origin, the cocaine-based products bought by consumers worldwide differ in significant ways.

Beyond the chemical nature of the primary psychoactive substance–which can take on two main forms (base and salt)–the variability also lies in the additives, impurities and residues present alongside cocaine; these factors taken together determine important properties such as the physical characteristics, possible routes of administration (mainly insufflation, smoking and injecting), the purity levels and the potential for harm. In practice, the derivation of the product is also crucial in order to fully understand its characteristics. Hence cocaine, as a drug, needs to be understood not just as a substance, but rather as a spectrum of products.

Authorities engaged in drug supply reduction and drug demand reduction must be wary of reducing cocaine products found in the illicit consumer markets to a single substance. The different forms of cocaine reflect, directly or indirectly, different realities in terms of the supply chain as well as the potential level of harm posed for health, and the threat can be best addressed if it is properly understood. It is important to appreciate that cocaine products undergo a chain of processing steps which often extends beyond the country of cultivation and even sometimes involves the consumers themselves. For instance, although crack [BR], crack [FCP] and coca paste (PBC) contain the same substance as their main psychoactive ingredient, their presence in a given country could suggest very different market dynamics.

In order to ensure that practitioners in drug supply and drug demand reduction fully appreciate these distinctions and their implications, and can capitalize on the insights they bring, there is a need for awareness raising and sensitization among relevant personnel. Moreover, records of seizures and other law enforcement interventions need to differentiate between the different cocaine products to the extent possible, and data collection mechanisms must be set up accordingly, so as to enable proper evidence-based strategies and programmes. In the absence of such reliable distinctions, there remains a risk that conflations and inaccurate naming of cocaine products will hinder the understanding of the cocaine market, and hence the response to its threat.

Forensic laboratories need to be adequately equipped, and have the capacity, not only to identify the presence of cocaine, but to profile the product holistically, including the chemical form (base or otherwise), purity levels, the nature of additives, trace alkaloids, solvent residues, isotope ratios, etc. These additional parameters provide a signature on the origin and history of the product, and may thus shed light on the country of cultivation, sequence of steps and methods used, and thus potentially on the routes and actors involved. Hence, understanding the nature of cocaine products ultimately helps to counter cocaine trafficking and the cocaine market. For example, some accounts point to an ongoing proliferation of certain stages of the production process of cocaine products beyond the countries where this activity is well-established. In order to confirm and fully understand this phenomenon, and to counter the associated threat, the collection, processing and dissemination of data on forensic profiles and production practices need to be refined to capture the differentiations between the different cocaine products outlined in this document.

For instance, systematically distinguishing between the various products containing cocaine in base form may shed light on the extent to which, and how, such products are being trafficked internationally to serve as starting material for processing in transit and destination countries.

Understanding and differentiating cocaine products and associated use patterns are equally important for demand reduction services in view of the different potential for harm associated with the various routes of administration and the various adulterants and residues.

There is a certain regional character to the global variability of cocaine products. It is no coincidence that the manufacturing process consumer products (MCPs) are mainly found in South America (close to the production areas). The fact that these products are mainly smoked may have rendered smoking a more common route of administration of cocaine than in other markets, and may have set the scene for the consumption of other smokable products in this region as well as in neighbouring Central America and the Caribbean. Thus, the apparent proliferation of cocaine processing activity, which seems to affect countries in Africa and Europe in addition to Latin America, has the potential to contribute to an expansion of the market of smokable products in these regions and to developments of use patterns similar to those in South America; this comes in the context of signs of an increase in the smoking of cocaine products (specifically crack [FCP]) in Europe.

Ultimately, a better differentiation of cocaine products in the international discourse on illicit drug markets will enable a better understanding of the phenomenon, an ability to interpret and anticipate the developments in the cocaine market and a more effective and more pre-emptive response to the problem.

Introduction

Cocaine consumption is a global phenomenon present in all world regions, albeit with varying degrees of intensity. In 2019, 20 million people were estimated to have used cocaine in the past year (UNODC, 2021a). Multiple indicators, ranging from cultivation to seizures and use, point to an ongoing expansion of the global cocaine market. Yet the understanding of this market is still uneven, with some aspects still subject to open questions, misconceptions, conflation of concepts and reliance on anecdotal information.

This document aims to shed light on what the cocaine consumer products are, including how they are prepared and what substances they contain, and in particular whether their main active ingredient is cocaine in the salt (typically hydrochloride) or the base form. However, this information alone is not sufficient and must be combined with information on how these products are consumed – the routes of administration used by consumers – as these have a critical bearing on the effects felt by the users and, crucially, the harms they may cause.

However, data are not available for all the affected regions and relevant products and those that are available are often difficult to access. In addition, the nature, quality, reliability and timeframe of the information available can vary, often widely, leading in particular to comparability issues. As a result, publicly available information on cocaine can sometimes be confusing or contradictory. And knowledge gaps remain in many world markets regarding the cocaine products available to users, in terms of their chemical form, purity, cutting agents used for dilution and adulteration, price and routes of administration. Both cocaine supply and cocaine demand are highly dynamic, marked by frequent shifts and changes. This has been especially visible in the early 2020s, where a combination of exceptionally high levels of cocaine production, intense growth in transportation and logistics chains globally (EMCDDA and Europol, 2019; 2016), a diversification of criminal actors involved in the supply chain from South America to Europe (UNODC and Europol, 2021b) and near-ubiquitous access to internet-based technologies has probably made more cocaine products available to more potential consumers in more countries than ever before.

The cocaine market is a considerable source of harms in terms of both security and health. In 2019, cocaine use disorders accounted for an estimated 1.15 million healthy years of life (DALYs) lost due to disability (559,000) or premature death (594,000) (IHME, 2021).

Cocaine use also contributes to the spread of infectious diseases through the sharing of smoking equipment as well as syringes, and as a risk factor for unsafe sexual behaviour (UNODC, 2017; Ti et al., 2011; Johnson et al., 2016).

Certain cocaine use patterns have been particularly associated with marginalization and poor socioeconomic conditions (UNODC, 2016b); they may also contribute to acquisitive crime and violent behaviour (UNODC, 2019c). In some countries along the cocaine trafficking routes, large-scale trafficking of the drug occurs in parallel with high levels of violence (UNODC, 2016b; UNODC, 2019c).

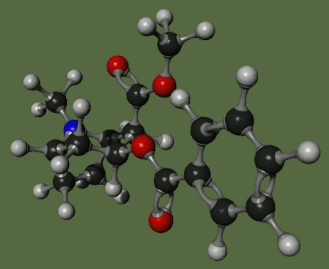
This report offers an overview of the cocaine consumer products available at global level. The illicit production chain is discussed insofar it sheds light on the consumer products. The report is based on available published evidence and on the knowledge gained through UNODC's monitoring activities in South American countries.

The report discusses briefly some chemical and pharmacokinetic aspects of cocaine, and then proceeds to define and discuss three main families of consumer products: manufacturing process consumer products (MCPs) derived from cocaine base and coca paste (PBC); freebase consumer products (FCPs) derived by converting cocaine salt back to base form; and consumer products based on cocaine hydrochloride (typically in powder form).

What is cocaine? Basic information

Cocaine is a natural substance occurring in the leaves of certain plants native to South America. Cocaine was placed under international control, along with the closely related substance ecgonine, by the Single Convention on Narcotic Drugs of 1961 as amended by the 1972 Protocol. While the convention defines the "coca bush" as any plant of the genus Erythroxylon, which is comprised of more than 250 species, cocaine is in practice extracted from the leaves of two cultivated species: Erythroxylon coca and *Erythroxylon novogranatense* (each of which occurs in two varieties).

Three-dimensional rendering of the cocaine base molecule



Cocaine belongs to the family of substances called alkaloids. From a strictly chemical point of view, "pure" cocaine may occur in two forms: base and salt. The cocaine base molecule ($C_{17}H_{21}NO_4$, benzoylmethylecgonine) consists of the "heart" of the drug and accounts for its psychoactive effects, which include a sense of physical and mental well-being, exhilaration and euphoria. Cocaine in base form is available on consumer markets in many world regions; it is mostly smoked. Cocaine salts consist of larger molecules and, theoretically, can come in several kinds, such as cocaine hydrochloride, cocaine nitrate, cocaine sulphate, and several others. However, in practice, cocaine hydrochloride is the salt which is most frequently encountered as an end-product sold to consumers. Cocaine sulphate may occur in the intermediate products of the cocaine production process.

Given that there are no indications of synthetic cocaine illicitly manufactured (or diverted) on any consequential scale, it may be assumed that the cocaine consumer products available on global markets have been manufactured from coca leaf. However, it is important to bear in mind that such products typically do not consist of a "pure" substance and therefore aspects such as impurities, physical characteristics and methods of production and consequent residues are part of their defining characteristics.

The cocaine production process

While this report focuses mainly on cocaine products which are consumed by users, the manufacturing process itself is important in understanding these consumer products. The process from coca leaf to cocaine hydrochloride, the main end-product ready for export in wholesale quantities, itself involves some intermediate products, namely coca paste (PBC) and cocaine base.

The manufacturing of cocaine hydrochloride is a dynamic, adaptive process that varies depending on the context in which it takes place. Geography, developments in agricultural methods, availability of the raw material and of the chemicals needed for the manufacturing process, drug trafficking routes and the presence of armed groups are some of the factors reported to have a major impact on how and where cocaine is produced in Bolivia, Colombia and Peru. How these factors combine at different times within particular regions in the three countries goes a long way to explain why different methods of cocaine production have been documented to exist.

That said, although the methods vary, all cocaine production processes are centred around 4 clearly differentiated products: coca leaf; coca paste (PBC); cocaine base; and cocaine hydrochloride (SIMCI, 2019b). All of these are commercial products, that is, they are bought and sold among actors of the cocaine manufacturing industry and one or several markets exist for each one of them. In this report, these products are referred to collectively as "products of the production process" in order to differentiate them from the "consumer products" sold to individual cocaine users that are reviewed in Section 3 of the present report. This section provides a brief overview of what is known about the 4 products of the production process.

The taxonomy used in this report relies on three major criteria: (1) the chemical form (base or salt) of cocaine present in the product; (2) the sequence of intermediate products from which the end-product is derived; (3) the specific methods and additional chemicals used to extract, convert, purify, adulterate and dilute the substance.

On the basis of criterion (1), the first major class of consumer products which can be identified are the hydrochloride-based powders. Aside from these, the consumer products containing cocaine in base form can be distinguished, on the basis of criterion (2), into two major classes, namely: the consumer products which are derived from intermediate stages of the production process from coca leaf to cocaine hydrochloride (the MCPs); and those which are derived from cocaine hydrochloride (the FCPs). Criterion (3) is then further used to distinguish between different FCPs and different MCPs.

FIG. 1 **The cocaine manufacturing process**

1) Additional steps may be required for some of the products sold to end consumers.

(2) In accordance with the laws in Peru and Bolivia, a legal market also exists for the sale of coca leaf for traditional consumption purposes. In the case of Colombia, production of coca leaf is aimed predominantly for the illicit production of cocaine; traditional use is limited.

Source: UNODC SIMCI, Colombia; elaboration based on various studies related to coca cultivation and the manufacture of cocaine hydrochloride.

Naming cocaine products for clarity

The information on cocaine products available in the literature is often ambiguous, unclear and can ultimately be confusing. A serious problem frequently encountered when attempting to describe cocaine products is the fact that products are named but that no definition of what they are is explicitly provided. The definitions are often left implicit, as if they were obvious and necessarily meant the same thing for everyone regardless of national particularities, cultural specificities and language.

In an effort to begin clarifying what the different cocaine products reviewed here are and are not, a specific terminology has been adopted in order to name as precisely as possible the different products identified in this report. The terminology complements the taxonomy of cocaine products, as described in Figure 2, to convey the nature of the products. The terminology is reflected in a typographical convention used throughout the report in an effort to remove some ambiguities. In the present report:

- Quotation marks (e.g. "crack", , 'Oxi') are used to mark words or passages as they appear in a bibliographical source and/or to indicate uncertainty as to the exact nature of the cocaine product between the quotation marks.
- Other terms (not in quotation marks) in a language other than English are in italics.

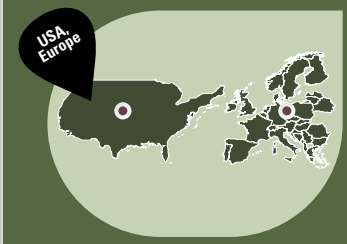
Moreover, the following nomenclature and typographical conventions have been adopted:

'Basuco' a street name used to refer to a range of mostly smokable MCPs found in Colombia and Venezuela

Crack [BR] refers to a smokable MCP found in Brazil

Crack [SA] refers to a smokable MCP reported by Colley and Casale (2014) to have been manufactured and sold to consumers for many years in Bolivia, Colombia and Peru

Crack [FCP] refers to a smokable FCP frequently found in the United States and Europe, among other markets



Merla refers to a smokable MCP found in Brazil

'Oxi' once erroneously said to be a new individual cocaine product, 'oxi' is a street name used to refer to a range of cocaine products available on the Brazilian market

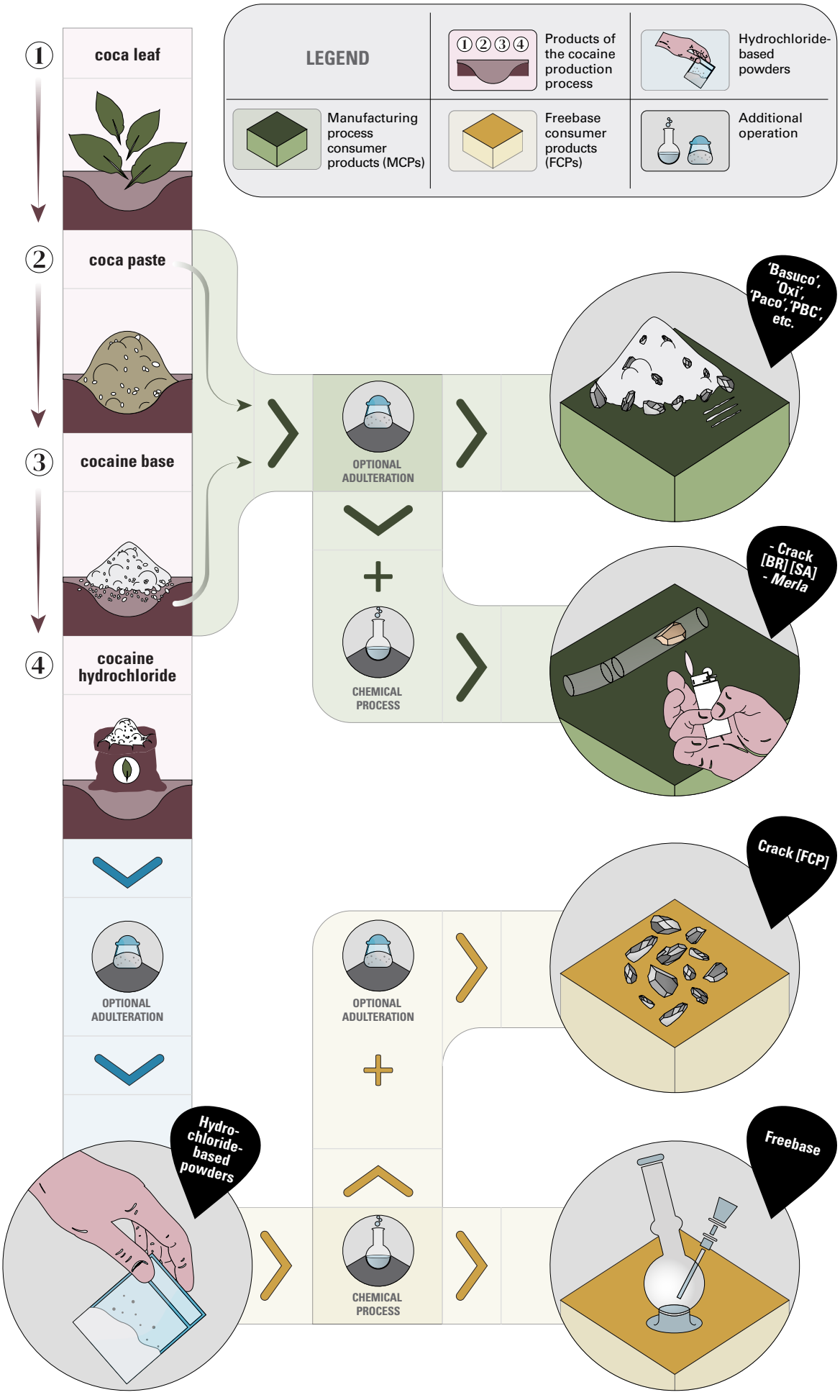
'Paco' a street name used to refer to a range of mostly smokable MCPs found in Argentina and Uruguay

'Pasta base' a street name used to refer to a range of mostly smokable MCPs found in several South American countries

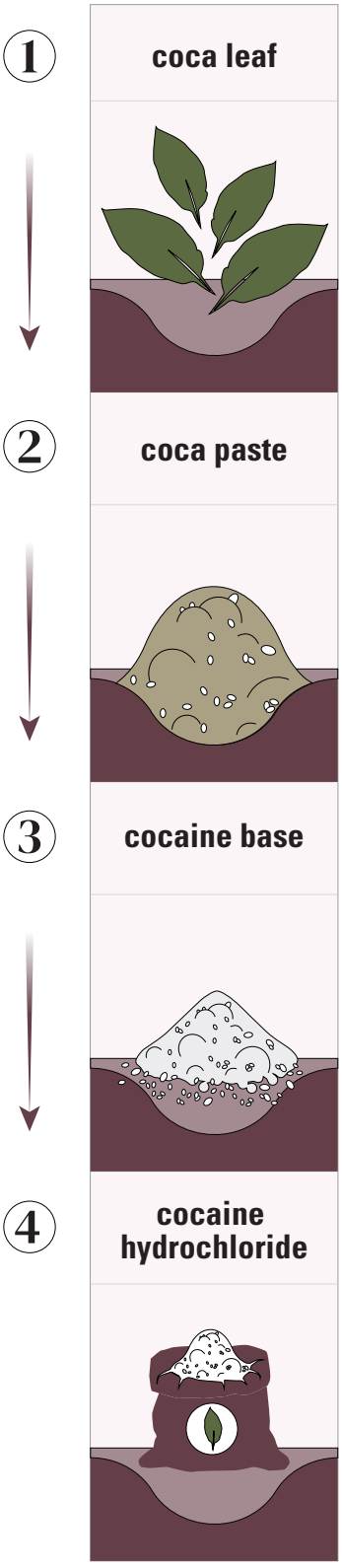
'PBC' a street name used to refer to a range of mostly smokable MCPs found in several South American countries

Coca paste (PBC) a product of the cocaine manufacturing process. Often also referred to as *pasta básica de cocaína*, or cocaine base paste– hence the acronym PBC.

FIG. 2 **Schematic representation of the relationship between the different cocaine products**



Products of the cocaine production process



The coca plant is the only natural source of cocaine. Aside from some wild-growing species whose leaves contain very small quantities of cocaine, the natural cocaine alkaloid is mainly found in the leaves of a range of cultivated varieties, or cultivars, of the plant that are grown mostly on the eastern slopes and valleys of the Andes and in some Amazonian lowland regions of South America (Plowman, 1981). However, cocaine is only one of several alkaloids present in coca leaves (Rivier, 1981).

Coca paste (PBC) is the first alkaloid-rich intermediary commercial product obtained when manufacturing cocaine hydrochloride from coca leaf (see Figure 1). Some sources (UNODC, 2016a; UNODC, 2012; ElSohly et al., 1991) refer to this product as "coca paste", but it is also frequently known as *pasta básica de cocaína* (PBC), or "cocaine base paste". However, the latter term can be misleading as this product may contain cocaine sulphate, which is a salt of cocaine (rather than a base). Nevertheless, given the widespread use of the term *pasta básica de cocaína*, this document henceforth refers to this product as "coca paste (PBC)".

It is sometimes also known as base paste (*pasta base*) (OUD, 2014). In Brazil, this product is known in Portuguese as *pasta base de cocaina* (Da Silva Júnior et al., 2012), or simply as *pasta base* (Campos Neto, et al., 2012). In Peru, the first alkaloid-rich product obtained when processing coca leaf has sometimes been called *pasta bruta de cocaína* or *pasta cruda de cocaína* ("crude cocaine paste").

Cocaine base is the second commercial intermediary product between coca leaf and cocaine hydrochloride (see Section on Chemical forms of cocaine below). It is obtained by purifying coca paste (PBC), and as a result its cocaine content is higher than that of coca paste (PBC), being estimated at about 80% in Colombia. Its sale price is superior to that of coca paste (PBC) (SIMCI, 2019b).

Within coca paste, cocaine is already present predominantly in base form,[1] alongside other substances. Some of these substances can be removed by the process of oxidation, which is achieved by adding a dilute acid and potassium permanganate to coca paste, yielding the purer product referred to as cocaine base. However, in Peru, purification of *pasta cruda de cocaína* has been reported to be most frequently performed with an alcohol, especially ethanol, and the resulting product is known as *pasta básica lavada* ("washed base paste") or *pasta base oxidada* ("oxidized base paste"),[2] or simply *base lavada* ("washed base") (Casale et al., 2008a).

Cocaine hydrochloride (HCl) is a salt that is produced by crystallisation of cocaine base with hydrochloric acid (see Section on Chemical forms of cocaine below). It is the end-product of the manufacturing process, and it is the main ingredient in the products commercialized globally, in myriad of different wholesale, semi-wholesale and retail markets.

1 Given the imperfect processes in clandestine operations, and variations in the production process, coca paste may also contain cocaine in salt form (cocaine sulphate).

2 UNODC Illicit Crop Monitoring Programme, Colombia (SIMCI).

Consumer products

This section focuses on what is known about the cocaine consumer products available in the different world regions in terms of chemical forms, routes of administration, range of products, purities and cutting agents used.

Chemical forms of cocaine products, routes of administration and basic pharmacokinetics

The cocaine alkaloid extracted and isolated from coca leaf is a chemical base (Benowitz, 1993). However, it is made available on world consumer markets in two chemical forms: as a base (with minimal solubility in water) and as hydrochloride salt (soluble in water) (Wexler, 2014).[3] A range of consumer products is derived from each of these forms.

Both chemical forms are readily absorbed through all mucous membranes of the body, including the mouth, nose, lungs, stomach and intestine (Karch and Drummer, 2015). Nonetheless, the chemical properties of each form partly determine the routes of administration available to users. In turn, routes of administration determine to a considerable extent the effects of cocaine on the body and the severity of the physical and psychological harms that can result from use (Karch and Drummer, 2015). By far the most frequently used routes of administration at global level appear to be the *nasal insufflation* ("sniffing", "snorting") of products in which cocaine is in hydrochloride salt from, and the inhalation of the vapours when products containing cocaine in base form are smoked.[4] The smoking of cocaine base products is likely to result in more harms to users than the snorting of the hydrochloride salt (Hatsukami and Fischman, 1996; WHO and UNICRI, 1995).

Cocaine base is readily smokable as it starts to vaporize at a relatively low temperature of around 90°C (UNODC, 2013; Dujourdy et al., 2010; Lizasoain et al., 2002; INCHEM, 1993). Consumer products containing cocaine base as the main psychoactive ingredient are smoked[5] in a variety of ways, including in ad-hoc pipes, in tobacco and cannabis cigarettes, through vaporization on an aluminium foil ("chasing the dragon"), in electronic cigarettes and using makeshift equipment improvised from common items such as cups and cans (Bastos and Bertoni, 2014; CICAD, 2014; UNODC, 2017; Release, 2020). By contrast, cocaine hydrochloride melts at 195°C, will decompose before vaporising and is thermolabile, meaning that it loses its properties when heated; therefore, it is not adapted for smoking (Colussi-Mas et al., 2003; Lizasoain et al., 2002; Benowitz, 1993; Stinus, 1992; Siegel, 1982)[6]. This goes a long way to explain why the most prevalent route of administration of cocaine hydrochloride is nasal insufflation.

Consumer products derived from cocaine base may appear in a diverse range of colours and textures (TNI, 2019; Henman, 2015), although the most commonly found products include off-white, grey or yellowish chunks of waxy, translucent solids often reminiscent of gravel or small rocks. This aspect is at the origin of some of the many different "street names" given to cocaine base products, including *pedra* in Portuguese, *piedra* and *roca* in Spanish, rock and gravel in English, *caillou* and *roche* in French, etc. The term "crack", probably the most widely known name of a cocaine base consumer product, originates in the popping sound often produced when heating cocaine freebase in order to smoke it. Although originally from the English language, the term "crack" is now used to describe cocaine base products in many non-English-speaking drug markets around the world.

The cocaine hydrochloride salt made available to consumers worldwide often appears as a white or off-white crystalline powder but may also presents itself as white shiny flakes or as a piece of solid material. Products based on the cocaine hydrochloride form are typically crushed into a fine powder before they are insufflated.

Being a salt, cocaine hydrochloride is readily soluble in water, and can therefore be injected in an aqueous solution. By contrast, cocaine base must be mixed with a weak acid such as vinegar or lemon juice in order to be dissolved and become injectable. When injected, both forms can be used on their own or in combination with other drugs, frequently heroin ("speedball"). In Europe, for instance, recent studies of residues in used syringes suggest that when cocaine is injected in combination with another drug, it is most frequently with heroin, although instances of cocaine combined with buprenorphine, methadone or, to a lesser extent, a cathinone were also found (EMCDDA, 2019a). In addition, cocaine hydrochloride and cocaine base may also be used orally, either by eating, rubbing against the gums or placing under the tongue.

While data on the route of administration of cocaine products are not systematically available at global level, the available data, mostly partial and indirect, indicate that nasal insufflation of cocaine hydrochloride and smoking

3 The solubility of cocaine base and cocaine hydrochloride in water are estimated at 0.17g per 100ml and 200g per 100ml respectively.

4 Based on data from 27 countries worldwide which responded to the relevant question in the UNODC Annual Report Questionnaire for 2019, the proportion of users who injected the drug was on average 8.7 per cent in the case of cocaine salts and 6.9 per cent in the case of "crack"[FCP].

5 In the mid-1980s, some users in the United States were reported to insufflate cocaine freebase nasally (Adams and Kozel, 1985). However, this was quite rare at the time and it has not been found reported as a method of cocaine base intake in recent years, although it is likely that some present-day users insufflate cocaine base without being aware that it is cocaine base (Dujourdy et al., 2010).

6 Casale and Klein (1993) note that the melting points of pharmaceutical grade cocaine base and cocaine hydrochloride are respectively 98°C and 195°C but that illicitly produced versions are likely to have lower melting points due to the presence of impurities.

of cocaine base products are the most common routes of administration, followed by injection and lastly by oral use.[7] Cocaine hydrochloride tends to be the most widely used cocaine product in most countries and, as mentioned previously, it does not lend itself to smoking. Moreover, the number of users of cocaine hydrochloride in a given country typically exceeds the users of any other cocaine product, and among these, only a minority inject (the same holds for users of other types of cocaine), leaving nasal insufflation as the primary route of administration of cocaine salts. Out of 14 countries worldwide[8] which reported prevalence of use of cocaine salts and at least one additional (smokable) type of cocaine through the UNODC Annual Report Questionnaire for 2019, the data for 13 countries indicated that the number of past-year users of cocaine salts was more than double the number of users of any other type.[9] Moreover, based on data from 27 countries worldwide which responded to the relevant question in the UNODC Annual Report Questionnaire for 2019, the proportion of users who injected the drug was on average 8.7 per cent in the case of cocaine salts and 6.9 per cent in the case of crack [FCP].

European data indicate that, among cocaine users entering treatment in 2018-19 who reported the main route of administration, 69% used nasal insufflation, 26% smoking (inhalation), 2.3% injection and 1.7% ingestion (EMCDDA, 2021).

The onset of action and the peak and duration of the effects depend on the dose administered and on the route of administration as these determine how much of the drug will enter the bloodstream and reach the brain, and how fast (Bono, 2008; Fattinger et al., 2000; Cone, 1995). However, the individual characteristics of users will also influence these factors (Fattinger et al., 2000; Cone, 1995). Compared to smoking and injection, nasal and oral administration are estimated to result in slower absorption of cocaine into the bloodstream and slower onset of action together with a later peak and longer duration of effects. Oral ingestion appears to have the lowest bioavailability of all routes, with 60% to 70% of the cocaine estimated to be destroyed by the body and producing no effects (Karch and Drummer, 2015; UNODC, 2013; Lizasoain et al., 2002; Fattinger et al., 2000). The effects of the remaining 40% to 30% peak within 30 minutes and last up to 2 hours. When cocaine is insufflated nasally, effects are estimated to occur within 1 to 5 minutes, peak in approximately 30 minutes and last for about an hour (Karch and Drummer, 2015; OFDT, 2012; Shannon et al., 2007; Lizasoain et al., 2002; Perez-Reyes et al., 1982). Estimates of the bioavailability of cocaine administered by the intranasal route reported in the literature vary widely between 25% and 80% (Fattinger et al., 2000), with a study reporting as much as 94% (Cone, 1995). However, since in many cases a proportion of the cocaine that is insufflated nasally is swallowed, it will not become bioavailable via nasal mucosa but via the digestive system, which complicates measurement of bioavailability via the nasal route (Fattinger et al., 2000; Cone, 1995).

By contrast, when cocaine is smoked or injected the effects are felt almost immediately and intensely, producing a euphoric feeling ("rush") that is much more intense than with the oral or nasal routes. The onset of action may occur slightly more rapidly after vapour inhalation (5 to 10 seconds) than after injection (15 to 20 seconds) but the effects are reported to peak within 3 to 5 minutes in both cases. When cocaine is smoked the effects appear to be relatively short-lived, lasting between 5 and 15 minutes, and are followed by a sharp drop ("crash") frequently leading to a craving for another dose; when injected their duration is longer at 20 to 60 minutes, but a "crash" effect is also often felt (UNODC, 2013; OFDT, 2012; Shannon et al., 2007; Lizasoain et al., 2002; Siegel, 1982).

In a study comparing the pharmacokinetics of different routes of cocaine administration, the average bioavailability of smoked cocaine was estimated at 70% (Cone, 1995). However, cocaine bioavailability when the drug is administered by smoking is heavily dependent on a series of factors, which may vary widely between individuals and even between smoking sessions by the same individual. These factors include the temperature of volatilisation of the cocaine and the amount of drug loss due to decomposition and to condensation, which in turn depend to a considerable extent on the type of smoking device used and on the skills and experience of the individual using it (Karch, 2008; Cone, 1995; Perez-Reyes et al., 1982; Siegel, 1982). As for the intravenous route, the biovailability of cocaine (as all drugs) is by definition 100% bioavailable (bioavailability is defined by how much of a substance enters the bloodstream (Karch, 2008)).

The available data indicates that nasal insufflation of cocaine hydrochloride is how a vast majority of users in Europe, North America and Oceania use the drug, with base smoking apparently restricted to a small minority. However, in the Caribbean and Latin America, while the data seem to broadly indicate that a majority of users also snort cocaine hydrochloride, there is evidence to suggest that a much larger proportion of users smoke cocaine base products than in other regions (CICAD, 2019a). Some sources even indicate that in some countries such as Bolivia, Chile, Colombia and Peru, the majority of cocaine users

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7 Cocaine may also be insufflated or rubbed in the rectum ("plugging"), vagina and penis, often in order to enhance sexual pleasure, but these routes are even less frequently reported than oral administration. Accidental administration of large amounts of cocaine in the bowels, rectum or vagina occasionally occurs in drug couriers transporting the drug intracorporeally, which may lead to fatal overdose (Karch and Drummer, 2015).

8 The geographical distribution of these countries was as follows: 6 in South America, 1 in Central America, 1 in North America, 1 in Asia and 5 in Europe.

9 In addition, the only 2 countries which reported data specific to cocaine products other than cocaine salts without reporting data specific to cocaine salts, provided aggregate data for cocaine in general which indicates that the users of the relevant "smokable" product comprised no more than a quarter of the cocaine-using population.

are smokers of base products, specifically MCPs as they are named in the taxonomy proposed above (see Figure 2) (SIMCI, 2019b; Comunidad Andina, 2013; CONACE, 2004). It should be stressed that, at global level, the number of users of products containing cocaine in base form is likely to be underestimated since many such users belong to sectors of the population that, for a variety of reasons, are underrepresented in surveys (Janssen et al., 2020). Evidence for the rest of the world is missing or patchy, making it challenging to provide a reasonably robust comprehensive description of the situation.

In any case, it is important to note that our image of the global distribution of cocaine products and routes of administration is likely to change in future as more of the drug becomes available globally. A likely consequence of the current cocaine wave is that some products and related routes of administration may emerge or expand in markets where they were previously absent or restricted to limited numbers of users and a narrower range of products. In this context, it will continue to be especially important to improve the research and monitoring of markets for cocaine base consumer products, especially since they are likely to be underestimated even as they may generate more harms than cocaine hydrochloride markets.

Cocaine base: a diverse range of consumer products

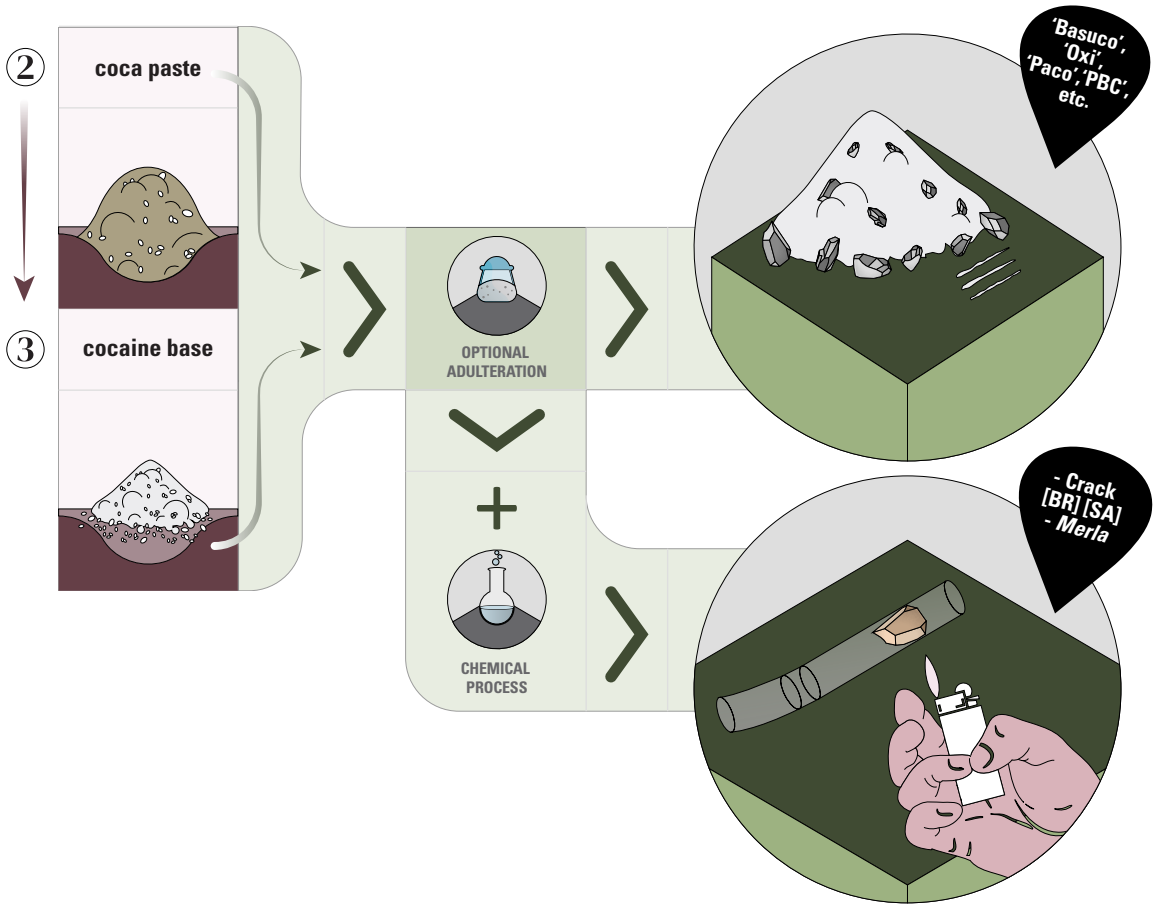
There is considerable ambiguity and confusion surrounding the consumer products where cocaine in base form is the main ingredient. Some issues arise because reliable, routine information on the composition of the products, and possible changes affecting them, is missing or is difficult to find due to a lack of routine forensic analysis in many countries or inadequate reporting and sharing of the results of such analysis. Much confusion is due to the fact that different terms are used in different markets to name what is essentially the same thing, such as 'basuco' in Colombia and 'paco' in Argentina. And, vice-versa, that the same name may be applied to what in fact are different products. For instance, the same word, "crack", is used in order to describe different products—an FCP found in many markets and MCPs found specifically in South America (see Figure 2, and relevant sections below). Also, it is not infrequent for media reports and law enforcement press releases to name products without any reference being made to their chemical composition, adding to the general confusion as to what name corresponds to what product. The picture is further blurred with media claims that a "new" smokable cocaine product has emerged when in fact it has not, as in the case of 'oxi' in Brazil.

The following two sections—on MCPs and FCPs—attempt to disentangle these issues with a view to clarifying the nature of the cocaine base consumer products currently available in different international drug markets. This is done primarily by identifying what cocaine ingredient they contain and how they were manufactured. Additional information on dilution, adulteration and methods of use is also provided where possible.

The categorisation of cocaine base consumer products (see Figure 2) proposed here rests on the analysis of recent forensic and other data and information from cocaine producing countries and major international consumer markets combined with a review of the international literature. Although an effort has been made to use recent data and information from as comprehensive a set of disciplinary, language and geographical sources as possible, some gaps persist. This is probably inevitable given the complex, dynamic and expanding nature of the present-day illicit global cocaine market, which makes current and comprehensive reporting on consumer products containing cocaine in base form a challenging endeavour.

The family of consumer products derived from cocaine in base form may be divided into two categories depending on the starting material from which they are prepared—the *Manufacturing process consumer products (MCPs)* and the *Freebase consumer products (FCPs)*. What makes the FCPs distinguishable from their chemical "cousins" the MCPs, is that they are prepared from cocaine hydrochloride, and not from one of the intermediary products such as coca paste (PBC) or cocaine base.

The manufacturing process consumer products (MCPs)



MCPs are made from coca paste (PBC) and cocaine base, the two major intermediary products occurring during the process of manufacturing cocaine hydrochloride from coca leaf (see Figure 2). In these two products, cocaine is predominantly in base form and thus amenable for smoking; indeed, the derived MCPs are primarily destined to be smoked and they are also known as "smokable cocaine substances" in English and "*cocaínas fumables*" or "*cocaínas de combustión*" in Spanish (CICAD, 2019a, 2016a, 2016b, 2014; Sedronar, 2015; Henman, 2015; TNI, 2019, Suárez et al., 2014; Castaño, 2000). Although smoking is by far the most prevalent route of administration used for these products, some South American users nevertheless inject them (Bastos and Bertoni, 2014; Suárez et al., 2014).

MCPs first emerged in Andean cocaine-producing countries some 50 years ago then spread to other regions of the Americas (TNI, 2019; UNODC, 2013; OGD, 1996; WHO and UNICRI, 1995). The information available suggests that the first MCP, then known as "coca paste", appeared initially in Peru in the early 1970s[10], then spread to Bolivia, Colombia and Ecuador, and subsequently to Chile and Argentina and probably Venezuela (TNI, 2019; CICAD, 2003; Castaño, 2000; OGD, 1996; Jeri et al., 1978). Some users in Caribbean island countries may also have experimented with MCPs in the 1980s (OGD, 1996; ElSohly et al., 1991), but it is now reported that crack[FCP] is the cocaine base consumer product most widely consumed in the region (TNI, 2019; OFDT, 2012; Klein, 2004; Ragoucy-Sengler et al., 2003; Jekel et al. 1994), although more detailed forensic evidence would be needed. During the 1990s and 2000s, MCPs further spread to Brazil, Paraguay and Uruguay and other South American countries, and probably to some Central American countries. However, it is reported that "crack" may be the most frequently used cocaine base product in Central America at present, but as is the case with the Caribbean, more evidence is required (CICAD, 2019a; 2016; 2014; 2003; Sedronar, 2019; Maldaner et al., 2016; Bastos and Bertoni, 2014; OUD, 2014; Santis et al., 2007; OGD, 1998; 1996; ElSohly et al., 1991; Cortés, n.d.).

It is possible that this spread was due, at least partly, to the relocation of some cocaine manufacturing activities out of the 3 principal Andean producer countries, which made the

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10 The early 1970s may be reported in the literature as the start of the emergence of MCPs because the first recorded clinical description of a patient presenting for issues related to "*pasta base*" consumption occurred in a Lima hospital in 1972 (Castaño, 2000), and the Peruvian police recorded its first seizure of "PBC" in the same year (UNODC, 2013). However, Henman (2015) suggests that the smoking of MCPs in Peru could have started in the 1950s or earlier.

products of the manufacturing process from which MCPs could be derived, namely coca paste (PBC) and cocaine base, available in locations where they previously did not exist (INCB, 2010; OGD, 1996). Although there is little evidence of this at present, there is a possibility of future further spread of MCPs to other regions where some stages of the cocaine hydrochloride production process occur and the raw materials are available, such as Central America, Mexico, Europe (EMCDDA and Europol, 2019; TNI, 2019) and Africa (Sidiguitiebe, 2016; Leggett, 2002).

What follows is a description of some of the main MCPs found on South American markets based on the evidence available from the literature. Not enough evidence has been found to even attempt describing products available in other Latin American regions, such as the Caribbean, Central America and Mexico. In these latter regions, more research and, in particular, forensic analysis, is clearly needed.

Although comparatively more data exists on South American MCPs, especially those available in Brazil, it should be stressed that finding reliable, comparable and stable evidence on the exact nature of the different MCPs reported to be sold on South American markets is a difficult task.

One factor contributing to this is the use of different names in different countries to refer to similar products. A related problem, that is also an indicator of the paucity of accurate information on the subject, is the widespread use in the literature of catch-all categories such "cocaine base paste", "PBC", "smokable cocaines" and other collective descriptors for several MCPs available in different South American countries, which in reality may or may not all be the same product.

This lack of precision and clarity is due in large part to a relative dearth of forensic evidence on MCPs, which in turn may be due to an absence of analyses or to poor or non-existent reporting of the results of existing forensic studies, or to both issues.

Although important knowledge gaps remain, the analysis of the literature indicates that the main products of the production process from which the various MCPs are prepared are coca paste (PBC) and cocaine base (see Figure 2).

Crack [BR] [SA]

In many countries, cocaine products may be found under the street name of "crack". As mentioned previously, the term "crack" originates in the popping sound often produced when heating cocaine freebase in order to smoke it. The main characteristics which are usually associated with products referred to as "crack" appear to be the fact that these products are smokable (hence the cocaine does not occur in salt form) and have a hard, non-friable consistency – often described as "rocks" (UNODC, 2016a; Zacca et al., 2014; CICAD, 2016b).

It appears however that there are important differences across countries, and likely also within some countries, between the products known as "crack", notably in the way they are derived – which is an important criterion used for the taxonomy adopted in this paper. In particular, it appears

that some – though not all - of the products marketed as "crack" in some countries in South America differ from "crack" as it is encountered in the main consumer markets of North America and Europe, in that they are derived from the base forms of cocaine (prior to conversion into hydrochloride), and hence are by definition MCPs according to the taxonomy of this paper. In contrast, the term "crack" as used in North America and in Europe generally refers to a product obtained from cocaine hydrochloride; in other words, a freebase consumer product (FCP).

Smokable products known as "crack" are commonly found on the consumer drug market of Brazil, where they have been available for several decades and given rise to much media attention and public concern (Ribeiro de Araújo et al., 2019; TNI, 2019; Bastos and Bertoni, 2014; Fukushima et al., 2014; Vieira Duarte et al., 2009; Mingardi and Goulart, 2002; WHO and UNICRI, 1995). "Crack" has been described in a fairly recent large epidemiological study as the most consumed smokable cocaine product in Brazil, ahead of "similar" products such as 'base paste', *merla* and 'oxi' (Bastos and Bertoni, 2014). More recently, Brazil has been described as the largest consumer market for "crack" in the world (Ribeiro de Araújo et al., 2019). A smokable cocaine consumer product with the street name "crack" is also reported to have been available in Uruguay since the early-2000s (JND, 2013)[11] and in Paraguay since the mid-2010s (CICAD, 2016a). Both are countries of the Southern Cone that share borders with Brazil.

While no precise description of the "crack" available in Paraguay and Uruguay has been found, the "crack" found in Brazil has been described briefly in Brazilian forensic studies as cocaine that has undergone a melting process followed by cooling and solidification. Hydrochloric acid and sodium carbonate (an alkaline substance) are mentioned in connection with this process (Zacca et al., 2014). The outcome is described as a solid that will be dried, packaged and sold to consumers in the form of small rocks (*pedra*) that can be smoked pure in pipes or crushed in tobacco or marijuana pipes or cigarettes (Zacca et al., 2014).

This source suggests that, in principle, the starting point for "crack" in Brazil could be any of coca paste (PBC), cocaine base or cocaine hydrochloride. However, forensic profiling by the Brazilian police forces indicates that, every year over 2012-2020, among samples taken from seizures of cocaine in base form and tested in the context of a dedicated project (Forensic Chemistry Service, PeQui project), the majority were consistently not oxidized, with this proportion reaching 97 per cent in 2020. In sharp contrast, among samples from seizures of cocaine in hydrochloride form in 2020, 97 per cent were classified as "highly oxidized" (BFP, 2021a). Moreover, it was assessed that, as of 2021, among the samples of cocaine in base form, at least 80 per cent exhibited characteristics of "crack" (as opposed to other products containing cocaine in base form, such as *merla*) (BFP, 2021b). These data suggest that most "crack" in Brazil has not undergone the oxidation step, and hence neither the transition to cocaine hydrochloride, and is thus derived directly from coca paste.

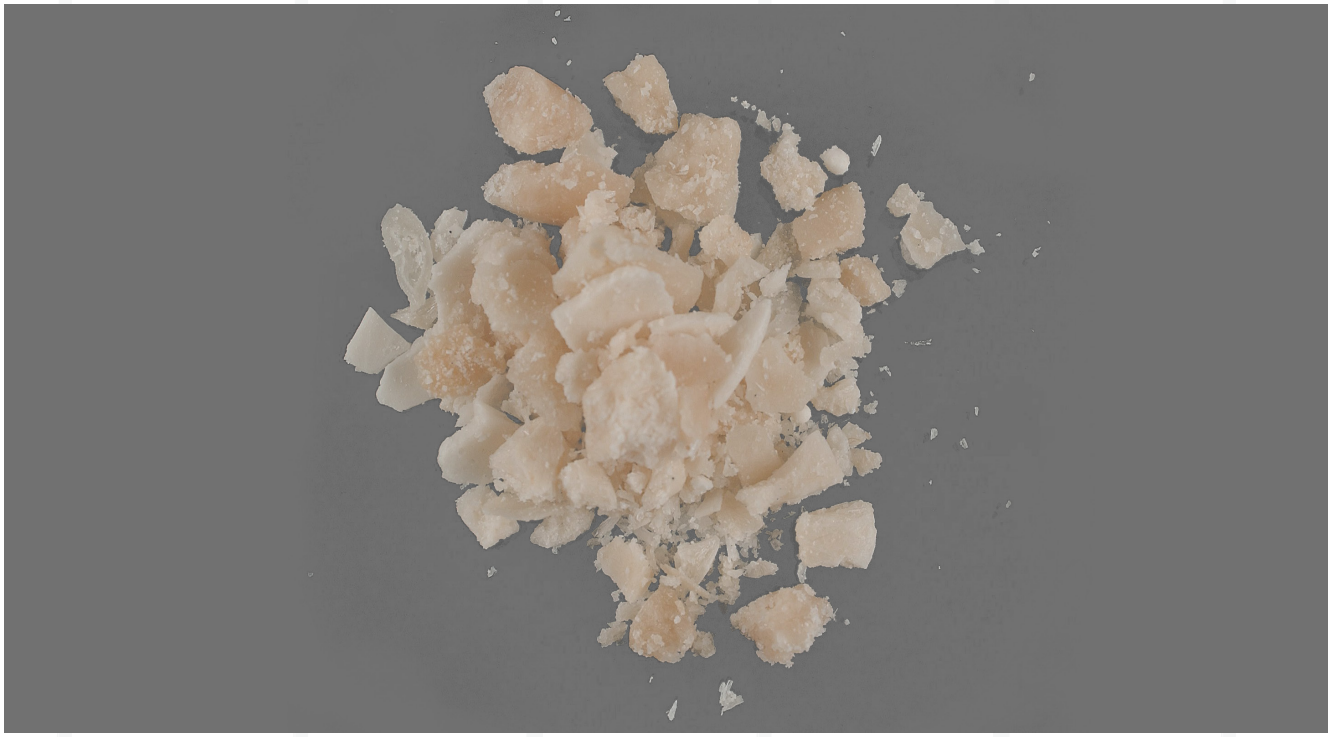
Other sources (CICAD, 2016b; WHO and UNICRI, 1995) confirm that the term "crack" in Brazil is used, at least sometimes, to refer to a product which is *not* derived from cocaine hydrochloride – although some of these also suggest that this exists alongside "crack" which is derived cocaine from hydrochloride (crack [FCP]). In this connection, it is particularly interesting to note that a joint report of the World Health Organisation (WHO) and the United Nations Interregional Crime and Justice Research Institute (UNICRI) states that two types of "crack" were available in the city of São Paulo, Brazil, in the 1990s: "*pedra*", made from coca paste (PBC) and thus an MCP; and "*casca*", made from cocaine hydrochloride, which is named "crack [FCP]" in the present report (WHO and UNICRI, 1995).

Thus, it appears that a significant portion – if not all – of "crack" marketed in Brazil corresponds to a product which is obtained from intermediate products of the cocaine production process rather than cocaine hydrochloride; that is, an MCP rather than an FCP. Henceforth the present document refers to this product as crack [BR]; however crack [FCP] may also exist in Brazil.

It is also important to note that large amounts of "melted cocaine" have been reported to be frequently seized at Brazilian borders in the form of 1-kilo bricks (Zacca et al., 2014). This could indicate that some of the products sold as "crack" to consumers in Brazil have been manufactured abroad, for instance in Bolivia, Colombia and/or Peru (Colley and Casale, 2014).

Indeed, a product described by American chemists as "South American crack" (henceforth denoted as "crack [SA]") is reported to be manufactured in Bolivia, Colombia and Peru. DEA chemists carried out a comparative analysis of samples of what they called "South American crack" seized in Bolivia, Colombia and Peru, and of "domestic crack" (henceforth denoted as "crack [FCP]") seized in the United States. According to Colley and Casale (2014), crack [SA] has been made for many years in the three cocaine producing countries "for local distribution and consumption". The two forms of crack examined in this study, [SA] and [FCP], were reported to be "easily differentiated" due to their distinct solvent profiles. The method reported by the DEA to be typically used in the three Andean countries in order to make crack [SA] is by "melting a crude cocaine base obtained directly from coca leaves through traditional illicit processing methods, skimming off the water and most water-soluble impurities, and allowing the cocaine base to cool and solidify" (Colley and Casale, 2014, p. 1). Similar methods were also briefly described elsewhere (TNI, 2019; Bastos and Bertoni, 2014; UNODC, 2013, Casale et al.

11 In Uruguay in the 2000s, crack was reported to be known to some users as "cooked cocaine" (cocaína cocida) (JND, 2013).



2008a; Malpica, n.d.). According to SIMCI, the method described by the DEA is known as "*fritado*" in Colombia, where it is used in order to rid coca paste (PBC) of humidity before it is sold on to cocaine base manufacturers.[12] As a result, the crack [SA] described by Colley and Casale may be what is known in Colombia as a specific form of coca paste (PBC), i.e. a product of the cocaine production process. The same product may therefore be sold for different purposes to either cocaine consumers or cocaine production actors.

It should be noted that Colley and Casale (2014) do not mention the use of acids or sodium carbonate in the method they describe, which may differentiate it from the method described by Zacca et al. (2014), although both methods involve some heating, cooling and solidification. Meanwhile, Zacca et al. (2014) do not report a solvent profile that could be compared to that reported by Colley and Casale (2014).

As a result, as far as manufacturing methods are concerned, the evidence does not allow to confidently establish that the two methods described respectively by the Brazilian and the American forensic chemists are different, although they certainly share similarities. Yet, although the crack [BR] found in Brazil and the crack [SA] found in Bolivia, Colombia and Peru, may or may not be manufactured using the same method, it is clearly established that both are manufactured from one of the intermediary products of the cocaine manufacturing process, and therefore that both are MCPs.

Given that several methods of making "crack" in South America could exist, two possibilities emerge that are not mutually exclusive:

- Firstly, it is possible that some of the substance described as crack [SA] by Colley and Casale (2014) and as dried coca paste (PBC) by SIMCI is smuggled from Bolivia, Colombia and Peru to other South American countries including Brazil where it is seized in 1-kilo bricks and retailed in the form of small rocks;

- Secondly, it is also possible that cocaine base is trafficked pressed into 1-kilo bricks from one or several of the three producing countries and then transformed into crack [BR] using the method/s described above in destination countries including Brazil.

For instance, trafficking of "base paste" has been reported to be fairly intense in the border areas between Brazil's Mato Grosso State and Bolivia (Campos Neto et al., 2012). And, as mentioned earlier, coca paste (PBC) is also reported to be exported from Peru to Ecuador, Bolivia, Brazil, Chile, Argentina and Uruguay, that is, countries where relatively large markets for MCPs exist (UNODC, 2013). Argentinian authorities report that "cocaine base paste" is often pressed into bricks before transportation (Sedronar, 2015). Some cocaine base is also reported to be seized in Brazil from international traffickers, particularly in the north-west of the country bordering Bolivia, Colombia and Peru (Da Silva Júnior et al., 2014).

Although "crack" is not reported as a name given to any cocaine consumer product commonly available in either Bolivia, Colombia or Peru, both crack [SA] and crack [BR] could nevertheless be sold to users outside Brazil under different names, such as 'basuco' in Colombia or 'paco' in Argentina and Uruguay, for instance. Unless specific forensic analysis allowing to determine how the MCPs available in South American consumer markets are prepared, for instance by establishing their solvent profiles, this will remain a knowledge gap.

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12 UNODC Illicit Crop Monitoring Programme, Colombia (SIMCI).

It may also be speculated that some of the consumer products that are sold as "crack" (CICAD, 2014) in Central American and Caribbean countries could in fact be MCPs prepared from coca paste (PBC) or cocaine base, as in Bolivia, Brazil, Colombia or Peru, and not FCPs prepared from cocaine hydrochloride as in Europe and the United States (See Figure 2). As in the case of South America, this will remain a knowledge gap until forensic analysis is performed on the "crack" available on the retail markets of Caribbean and Central American countries.

Finally, it is of course probable that crack [FCP] (see Figure 2) is manufactured from cocaine hydrochloride in South American countries including Argentina (TNI, 2006), Brazil (Fukushima et al. 2014; WHO and UNICRI, 1995), Colombia (TNI, 2019; Molina, 2014), Paraguay (CICAD, 2016a), Peru (Henman, 2015) and Uruguay (JND, 2013), where it would be available to consumers in addition to MCPs. However, reports of crack [FCP] being available to consumers in South America are infrequent, and none of those mentioned earlier in this paragraph are based on forensic evidence.

In summary, the available evidence indicates that a certain MCP - crack [BR] - consisting of a solid, non-friable form of cocaine base, and derived from coca paste (PBC) (a product of the cocaine manufacturing process), exists in Brazil. The crack [BR] found in Brazil may or may not be manufactured in the same way as the crack [SA] made in Bolivia, Colombia and Peru. But in any case, the crack [BR] made in Brazil and the crack [SA] made in Bolivia, Colombia and Peru may be neatly differentiated from the crack [FCP] available in other markets such as North America (and Europe) because the latter has a different solvent profile, is prepared from cocaine hydrochloride and hence is a freebase consumer product (FCP) according to the taxonomy proposed here.

Merla

Merla is a cocaine smokable product that has been available on the Brazilian consumer market for several decades (TNI, 2019; Vieira Duarte et al., 2009), especially in the centre and north of the country (Zacca et al., 2014; Neves, 2013; Blickman, 2006). Medeiros et al. (2009) indicate that *merla*, also known as "*mela*" and "*mescla*" (mixture in Portuguese), used to be the name given to the residual sediment left following the processing of coca leaf into coca paste (PBC) and that contained a small amount of cocaine, but that subsequently the name *merla* came to be applied to a consumer product that is different from residual sediment. A similar transfer of the name initially transferred from a cocaine manufacturing by-product to a range of consumer products appears to have taken place in the case of 'basuco' in Colombia.

Prevalence of *merla* use appears to have declined in Brazil in recent years (Zacca, et al. 2014), and in the last national survey available it is reported to be lower than use of other smokable cocaine products such as crack [BR], "pasta base" and 'oxi' (Bastos and Bertoni, 2014) (See Section on 'oxi' below). Use of *merla* is reported to be more prevalent outside of Brazilian state capitals than in these larger urban settings (Bastos and Bertoni, 2014). *Merla* has not been reported to be a name used to describe cocaine products available to consumers outside Brazil in the literature reviewed here.

Several descriptions of *merla* can be found in the literature, and all concur that the product most often is sold to consumers in the form of a wet, whitish or yellowish paste, which is smoked, frequently mixed in tobacco or marijuana cigarettes (De Souza, 2014; Zacca et al., 2014; Neves, 2013; Medeiros et al., 2009; Blickman, 2006; TNI, 2006). Forensic analysis of *merla* indicates that it contains cocaine in base form, large amounts of water (up to 70%) and of sodium salts including sulphate, carbonate and bicarbonate, and residue of the manufacturing process of coca paste (PBC) or of cocaine base (Zacca et al., 2014; Neves, 2013; Medeiros et al. 2009).

According to a summary description reported by Brazilian forensic scientists, *merla* may be obtained from both coca paste (PBC) and cocaine base treated with a solvent, for instance a paint thinner, sulphuric or hydrochloric acid and sodium carbonate. Heating is not reported to be required in the preparation of *merla* (De Souza, 2014; Zacca et al., 2014; Neves, 2013). Forensic profiling of 30 samples in the late 2000s indicated that cocaine concentrations in *merla* can vary widely and that it is likely that the product is manufactured in Brazil (Medeiros et al. 2009), probably from imported coca paste (PBC) and cocaine base as no reports of international trafficking of *merla* have been found in the literature.

In summary, the available evidence indicates that the consumer product called *merla* is a manufacturing process consumer product (MCP), and namely a wet paste form of cocaine base made in Brazil from imported coca paste (PBC) and/or cocaine base. *Merla* appears to be available in Brazil only, where it is sold to be smoked on its own or mixed with tobacco or cannabis herb. However, it is possible that similar pasty smokable cocaine products are sold under different names in other South American countries, for example some of the products sold as 'basuco' in Colombia (UNODC and OAS, 2014). The Brazilian Federal Police (Forensic Chemistry Service, PeQui project) commented that, as of 2021, samples of *merla* were rarely encountered and *merla* had been supplanted by crack [BR] in the illicit market in Brazil (BFP, 2021b).

'Oxi'

'Oxi', also known as "*oxidado*", was first reported and described as "possibly one of the most potent and dangerous drugs known" and "a variant of crack" smoked by users in the State of Acre, in the Amazonian north-west of Brazil,

by a harm-reduction organisation and a news media in May 2005 (Viana, 2005). Although the news caused some alarm in Brazil and neighbouring countries at the time, it was subsequently forgotten (Da Silva Júnior et al., 2012). However, in late 2010 and during 2011, alarming news concerning 'oxi' reappeared in the Brazilian media and in some international scientific publications (Bastos et al., 2011), where it was again presented as a "new" and "highly potent" smokable cocaine product. 'Oxi' was described as a product related to crack [BR] but different from it since 'oxi' preparation was said to involve calcium oxide and a fuel such as kerosene or petrol. Moreover, 'oxi' was said to be cheaper than crack [BR] because it was made from residue and by-products of crack [BR] preparation (see also CICAD, 2014).

However, a Brazilian forensic study has shown that these reports were not based on facts, and specifically that 'oxi' was not a new drug but simply a name given to a range of existing cocaine products arbitrarily categorized as 'oxi' (Da Silva Júnior et al., 2012). Twenty samples seized at retail level and officially classified as 'oxi' by the Civil Police of the State of Acre, and 23 samples seized in Acre from interstate or international traffickers by the Brazilian Federal Police were chemically profiled. Six of the samples submitted by the Acre police (20%) were found to be cocaine hydrochloride, which is a non-smokable cocaine product. These samples were not further analysed as they could not possibly be 'oxi', a smokable, allegedly new product. Analysis of the remaining 14 samples provided by the Acre Police showed that 4 were crack [BR], 7 were coca paste (PBC) and 3 were cocaine base. Half of these 14 samples contained the adulterant phenacetin in varying amounts, and no other adulterant was found. Thirteen of the samples submitted by the Federal Police proved to be coca paste (PBC) and the remaining ten were cocaine base, with 5 of the 23 samples containing phenacetin. No diluents were found in either set of samples and the purity of a majority of the samples was quite high, ranging between 40% and 80%, with a few samples above 90% (Da Silva Júnior et al., 2012).

The case of 'oxi' appears to be similar to the media hype surrounding the amphetamine tablets sold in the Middle-East as "captagon" that occurred in much of the world following the terrorist attacks of November 2015 in the Paris region (Laniel, 2017). In both cases, lack of reliable information about the exact composition of a drug product that is assumed to be new or specific due to its "street name", led to misleading speculations and unnecessary public concern. The case of 'oxi' illustrates again the centrality of reliable forensic information to the understanding of drug markets.

In summary, 'oxi' is not a cocaine product. It is a "street name" used in Brazil by some official, media and civil society organisations to describe a range of other cocaine products including cocaine hydrochloride and MCPs.

'Basuco'

Originally, 'basuco' (sometimes spelt *bazuco*) used to be the name given to the residue of the processing of large quantities of cocaine. The name is often said to be an abbreviation of the phrase *basura sucia de cocaína* (dirty cocaine trash) (e.g. TNI, 2019), but since the suffix *uco* is often used in Spanish to form derogatory words from nouns and adjectives 'basuco' may simply be understood as a pejorative form of the noun, *base* (*de cocaína*) (Sabogal and Urrego, 2012).

At present, 'basuco' is a name given to smokable cocaine consumer products available in Colombia and in Venezuela (Sabogal and Urrego, 2012; Dávila et al., 2001)[13], but Colombia is the only country for which enough information has been found. Use of 'basuco' is associated in Colombia with urban poverty and other social problems such as homelessness, and the drug is generally perceived by both its users and the public as a "dirty" drug made of toxic by-products of cocaine manufacturing (Molina, 2014).

Colombian consumers are reported to smoke 'basuco' most often mixed in tobacco or cannabis cigarettes although it can also be smoked in pipes (Sabogal and Urrego, 2012). 'Basuco' has been described alternatively as a dry solid that may appear as a rough powder or as a small rock (TNI, 2019; 2006; Sabogal and Urrego, 2012), or as a damp substance (UNODC and OAS, 2014), both of which may be of different colours (white, off-white, yellowish, greyish, brownish).

It is also reported that the chemical composition of 'basuco' is variable. Thus, a forensic analysis of 109 representative samples of 'basuco' seized in Colombia in 2010 showed that caffeine and, to a lesser extent, phenacetin were the most commonly found adulterants (Sabogal and Urrego, 2012). The cocaine content of the samples was reported to vary widely between 4% and 70%, although a majority of samples was found to contain cocaine in concentrations of between 20% and 50% (Sabogal and Urrego, 2012). A more recent study of a smaller number of samples of 'basuco' (n=16) and cocaine hydrochloride (n=12) consumer products collected by a harm-reduction organisation in Bogotá, Colombia, in July 2014, has found a similar combination of adulterants in 'basuco' and confirmed its relatively high purity (38.8% on average) (Molina, 2014). Molina (2014) also indicates that residues of the fuels (e.g. kerosene), acids (e.g. sulphuric acid) and potassium permanganate used to manufacture the starting materials of 'basuco' (see Section on Products of the manufacturing process above) may also be found in 'basuco'. It is also worth mentioning that the study found that 'basuco' samples contained more cocaine and smaller amounts of a narrower range of adulterants than cocaine hydrochloride samples (Molina, 2014). Similarly, an analysis of a small number of "coca paste" samples seized in Bogotá in the early-1990s

13 'Basuco' is also reported to have been found as an adulterant in tablets sold as ecstasy in Colombia (Comunidad Andina, 2013).


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found significant amounts of fuel and potassium permanganate residues and high cocaine concentrations in the samples (ElSohly et al., 1991).

It is impossible to ascertain that 'basuco' is a specific product since there seems to be no consensual definition of the term in the literature reviewed here. Most sources do seem to agree, however, that 'basuco' is either prepared from coca paste (PBC) (see Figure 2) or is itself coca paste (PBC) in dry or damp form, with adulterants reported to be added in both cases (TNI, 2019; CICAD, 2016a; 2014; Fischer et al., 2016; UNODC and OAS, 2014; Comunidad Andina, 2013; UNODC, 2013; Sabogal and Urrego, 2012; TNI, 2006; Castaño, 2000; Malpica, n.d., etc.). Cocaine base (see Figure 2) is very rarely mentioned as potential starting material for 'basuco' in Colombia, although the cases of crack [BR] and *merla* reviewed above make it clear that this could be an option (De Souza, 2014; Zacca et al., 2014; Neves, 2013), as does the presence of potassium permanganate residue.

The reliability of this information is difficult to assess since, unlike crack [BR] and *merla* in Brazil and the South American crack [SA] described by the DEA (Colley and Casale, 2014), no description of 'basuco' preparation methods has been found anywhere in the literature, and there are apparently no reports on the solvent or alkaloid profiles of this product. This may be because no specific forensic studies have been performed (or their results reported).

Thus, in the early 2010s, Sabogal and Urrego (2012) explained that although Colombian authorities differentiated between coca paste (PBC), cocaine base, 'basuco' and cocaine hydrochloride when they reported seizures[14], the criteria that they used in order to distinguish between the products were not based on chemistry but on visual and contextual aspects. These included whether a seized substance appears as a finished product (for instance, a consumer product of about a gram wrapped in a piece of newspaper; or a larger amount of a dry substance compacted as a brick); and the locale and circumstances of the seizure. Importantly, the authors explained that the Colombian authorities reported that due to "laboratory limitations" it was not possible to differentiate between coca paste (PBC), cocaine base and 'basuco' in other ways (Sabogal and Urrego, 2012).

It should also be observed that none of the various reports about smokable cocaine consumer products, including 'basuco', in South America published after 2014 that have been reviewed here contains any reference to the forensic study by Colley and Casale (2014) reporting that "South American crack" [SA] has been made in Bolivia, Colombia and Peru "for many years". This is surprising since there is a strong probability that some of the products sold as 'basuco' in Colombia (and Venezuela) could in fact be crack [SA] ("South American crack"), especially in view of the fact that no other product reported seized or consumed in the country could fit the description of crack [SA].

In summary, 'basuco' is in all likelihood a "street name" used to describe a range of different smokable cocaine substances available on the Colombian (and Venezuelan) consumer markets. Neither a clear definition of 'basuco' nor any description of how such a product could be made was found in the literature. In this sense, 'basuco' would be similar to 'oxi' in Brazil (see above). The available evidence further suggests that the products collectively referred to as 'basuco' are MCPs (See Figure 2) that contain a fairly large amount of cocaine and that are adulterated mostly with caffeine and phenacetin. Although there is not enough forensic evidence to draw definite conclusions, it is likely that the term 'basuco' as used in Colombia covers the following consumer products:

- Coca paste (PBC), dried or damp, sometimes adulterated with caffeine and phenacetin;
- Cocaine base, dried or damp, sometimes adulterated with caffeine and phenacetin;
- Crack [BR] and crack [SA], as described in Brazil and in Bolivia, Colombia and Peru, sometimes adulterated with caffeine and phenacetin.

Additionally, *merla*, as described in Brazil, may also be one of the products sold in Colombia under the name 'basuco', while crack [FCP] made from cocaine hydrochloride may also be sold and/or prepared by users in Colombia.

14 The Colombian Drug Monitoring Centre recently reported seizure statistics where 'basuco' is differentiated from cocaine hydrochloride and a category called "cocaine paste/base" but did not explain how the distinction was made (ODC, 2017). SIMCI (2019b) uses similar categories.

'Paco', 'pasta base', 'PBC', etc.

'Paco' is a street name frequently used to describe a range of manufacturing process consumer products (MCPs) that is mostly smoked in home-made pipes since the early-2000s by consumers in Argentina and Uruguay (JND, 2019; TNI, 2019; 2006; CICAD, 2016a; Moraes et al., 2015; Sedronar, 2015; 2007; Arias et al., 2014; Súarez et al., 2014; Capece, 2008; Míguez, 2008). The term is likely to be an abbreviation of *pasta de coca* ("coca paste") or of *pasta de cocaína* ("cocaine paste").

Many sources addressing Argentinian and Uruguayan drug issues equate 'paco' and terms such as *pasta básica de cocaína* or *pasta base de cocaína*, also often mentioned by the acronym "PBC", and other terms including "PBC seca", "pasta base", "pasta", "base", together with many other "variations on the *pasta* theme" as Henman (2015) has aptly put it. These products are also reported to be smoked, both mixed with tobacco or marijuana, or pure using home-made pipes[15] (CICAD, 2019a; 2019b; 2016; 2014; JND, 2019; 2013; 2006; TNI, 2019; 2006; Moraes, 2015; Moraes et al., 2015; Prieto et al., 2015; Sedronar, 2015; 2007; Arias et al., 2014; Súarez et al., 2014; OUD, 2014; Ralón et al., 2012; López-Hill et al., 2011; Pascale et al., 2010; Prieto and Scorza, 2010; Capece, 2008; Míguez, 2008).

In turn, many sources dealing with drug markets elsewhere in Latin America also use PBC (or the English acronym, CBP), *pasta base* and similar variations to describe MCPs available in other countries including Belize, Bolivia (*pitillo*), Brazil, Chile (*mono*), Colombia (*basuco*), Ecuador (*baserolo*), Guatemala, Nicaragua, Panama, Peru (*pay*), Paraguay (*chespi*) and Venezuela (CICAD, 2019a; 2019b; 2016; 2014; TNI, 2019; 2006; Henman, 2015; Duffau et al., 2014; UNODC and OAS, 2014; Comunidad Andina, 2013; UNODC, 2013; Santis et al., 2007; Dormitzer et al., 2004; Lizasoain et al., 2002; Dávila et al., 2001; Castaño, 2000; Jeri, 1984).

Therefore, it appears that 'paco', 'pasta base', 'PBC' (CBP), and the other "variations on the *pasta* theme" including 'basuco', are all equivalent terms used in order to describe the various MCPs available on different Latin American consumer markets.

Furthermore, the names suggest that all these consumer products consist in coca paste (PBC) of varying cocaine alkaloid concentrations and adulterant contents (eg. UNODC, 2013). However, except in the case of crack [SA], crack [BR] and *merla* in Brazil, no description of how these products are prepared has been found in the literature. Importantly, no forensic evidence has been found in the literature confirming that the products thus named are *not* prepared from substances other than coca paste (PBC), such as cocaine base for instance. On the contrary, there are indications that in Peru, several types of 'PBC' are available to users, one of which is called *PBC lavada* and is described as a product ready for use in order to manufacture cocaine hydrochloride (UNODC, 2013). Similarly, Henman (2015) reports that several grades of "pasta lavada" are available on the consumer market in Lima. This is likely to be cocaine base.

Similarly, no evidence has been found that would exclude the possibility that some of these products could be crack [SA] (Colley and Casale, 2015), crack [BR] or *merla* as described in Brazil (Zacca et al., 2014; Neves, 2013; Medeiros et al. 2009)[16]. Yet, forensic studies in Brazil have shown that crack [BR] and *merla* may be prepared alternatively from coca paste (PBC) or cocaine base, and there is evidence indicating that "melted cocaine", coca paste (PBC) and cocaine base are smuggled from cocaine producing countries into Brazil. And it would be very surprising if this were not also the case in other countries both near (Argentina, Paraguay, Uruguay, Venezuela) and further away (Belize, Chile, Ecuador, Guatemala, Nicaragua, Panama) from Brazil, especially since most share borders with Bolivia, Colombia and/or Peru.

In summary, it is likely that the terms 'paco', 'pasta base', 'PBC', etc., as used in many Latin American countries are, like 'basuco' in Colombia, street names describing a range of different MCPs. Although there is not enough forensic evidence to draw definite conclusions, it is likely that these terms as they are used in the literature cover in reality the following consumer products (see Figure 2):

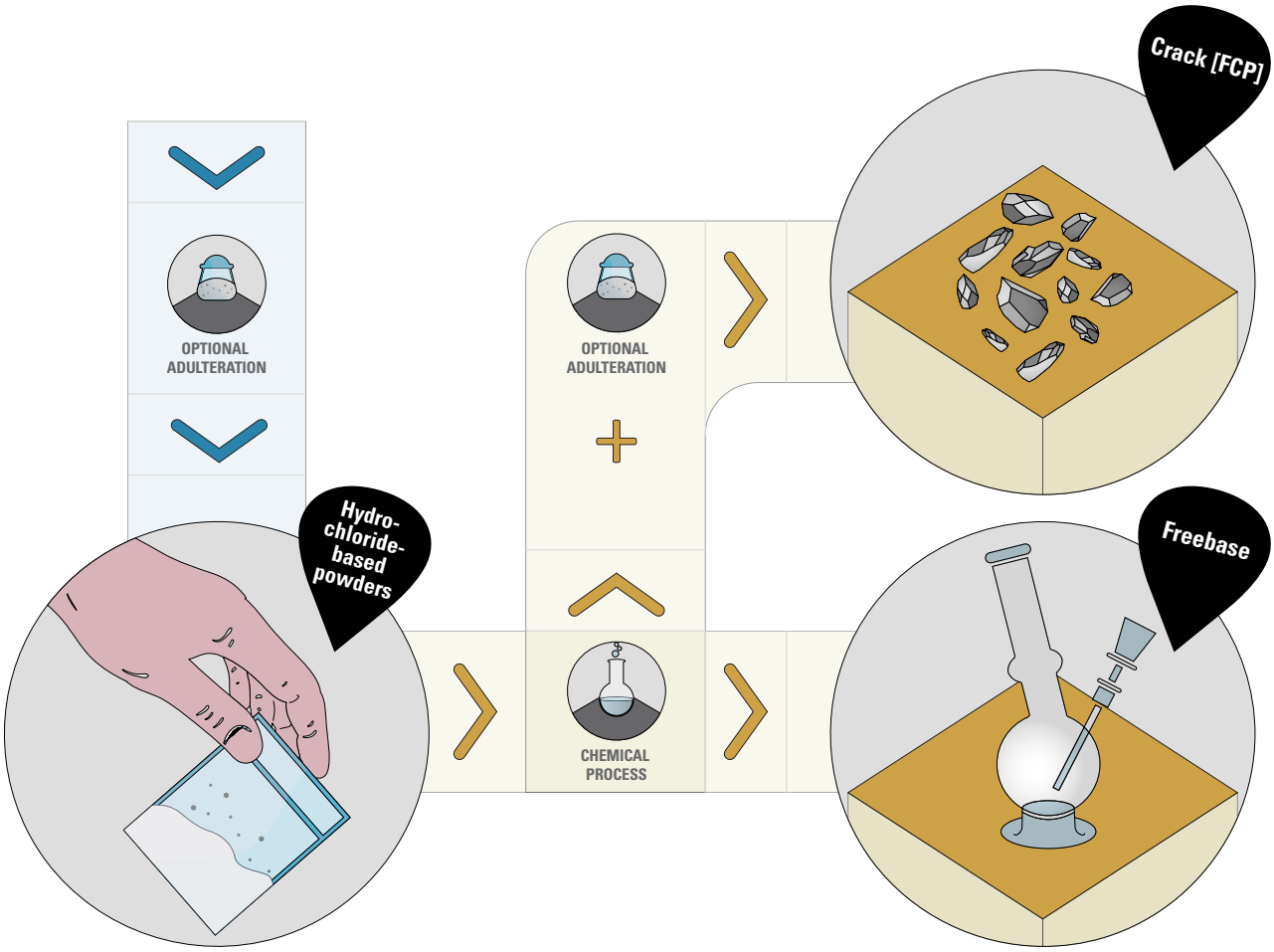
- Coca paste (PBC), dried or damp, sometimes adulterated with caffeine and phenacetin;
- Cocaine base, dried or damp, sometimes adulterated with caffeine and phenacetin;
- Crack [BR] and crack [SA], as described in Brazil and in Bolivia, Colombia and Peru, sometimes adulterated with caffeine and phenacetin.

In addition, *merla*, as described in Brazil, and crack [FCP] prepared from cocaine hydrochloride (see section of FCPs below) may also be sold under different names or prepared by users in Latin America.

15 The UNODC (2013, p. 54) provides a detailed description of the preparation and smoking of a mixture of PBC and tobacco in a cigarette in Peru. Photographs of different home-made pipes used in Colombia and Argentina can be seen in the reports of the Transnational Institute (TNI, 2019) and Sedronar (2015).

16 Use of "crack" is reported by the Inter-American Drug Abuse Control Commission in its last report on drug use in the Americas to occur in 8 South and Central American countries, in 4 Caribbean countries, in Mexico and in the United States (CICAD, 2019a). However, since CICAD (2019a) does not provide a precise definition of "crack", it is probable that this covers crack [FCP] prepared from cocaine hydrochloride and crack [SA] prepared from coca paste (PBC) or cocaine base. The CICAD (2019a) report does not include information on drug use in Brazil.

The cocaine freebase consumer products (FCPs)



Two FCPs have been identified: freebase and crack [FCP], and both are primarily destined to be smoked, although some users inject them. Both are prepared by subjecting cocaine hydrochloride to relatively straightforward chemical processes using a weak base in order to transform the cocaine hydrochloride salt into a base form that has been freed of hydrochloric acid, hence the name "freebase". The main difference lies in the final stages of the processes which, in the case of freebase, involve an additional extraction step by means of an organic solvent (e.g. diethyl ether), which results in the elimination of certain types of impurities.

These processes mentioned above are sometimes referred to as "freebasing" in English (Freye, 2009; OGD, 1996; Bean, 1993), although the same term has also been applied to the smoking of cocaine in freebase form (Gootenberg, 2008; Karch, 2008; Castaño, 2000; Farrar and Learns, 1989; Manschrek et al., 1988). In Latin American Spanish, transforming the cocaine hydrochloride salt into a base form is sometimes colloquially referred to as "patraseo" or "patraceado" meaning literally "turning back" or "sending back" (TNI, 2019; CICAD, 2016a; UNODC 2013; Molina, 2014; Castaño, 2000).

As in the case of the MCPs reviewed above, much of the data and recent information available about the FCPs appear to be characterised by ambiguity, lack of precision and problematic availability. A difficulty arises out of the fact that some datasets and reports do not discriminate between the hydrochloride and freebase forms, conflating both under the same heading of "cocaine" (EMCDDA, 2019b; SAMSHA, 2019; DEA, 2019; 2015), while others group cocaine hydrochloride, FCPs and MCPs together (UNODC, 2019b). In addition, in spite of notable exceptions (CICAD, 2016a; UNODC, 2013; Colussi-Mas et al., 2003; Castaño, 2000; Perez-Reyes et al., 1982; Siegel, 1982), the literature infrequently differentiates between crack [FCP] and freebase since they are chemically the same form of the drug, and some conflate MCPs and FCPs as they all are types of smokable cocaine.

FCPs users themselves may also confuse products and/or altogether misconceive what they actually contain, with a probable impact on the data collected by international organisations. In Paris, for instance, where most crack [FCP] use in mainland France is concentrated, users view crack [FCP] as a "dirty" drug made with sodium bicarbonate and waste product from the cocaine manufacturing process. And they are convinced, erroneously, that what they call "freebase" is a pure product because it is made with cocaine hydrochloride and ammonia (see below section on Freebase). A compounding factor is that

Preparation of crack [FCP]: the misconception of using ammonia

In Paris in 1993, the French monitoring centre for drugs and drug addictions (OFDT) carried out a study in which it tested the purity of a purchased sample of cocaine hydrochloride and of a set each of crack [FCP] and so-called "freebase". Each set was prepared, for the purposes of the study, from the same purchased sample of cocaine hydrochloride by different users with some using sodium bicarbonate and others ammonia. The study found that both ammonia and sodium bicarbonate resulted in a somewhat purer product than the starting cocaine hydrochloride material and that similar purities were observed regardless of whether sodium bicarbonate or ammonia was used. It also found that most of the cutting agents present in the starting material were present in the end product, proving that users' perceptions were disconnected from the reality of the products (OFDT, 2013) (see below section on Freebase). A similar disconnection between users' perceptions of product quality and the actual composition of products available on the French market as revealed by chemical analysis was also encountered in the case of heroin (Dujourdy and Besacier, 2010).

in Paris crack [FCP] tends to be purchased ready-made from dealers, while "freebase" is often home-made by its users, who enjoy a certain prestige among their peers as a result. The upshot is that at least some FCP users in France are confident that what they inhale is freebase, and they neither view nor report themselves as crack [FCP] users but as cocaine users when they seek treatment or participate in surveys. Much of their reluctance to view themselves as crack [FCP] users has to do with the negative image of crack [FCP] due to its perceived negative effects on health and socioeconomic status (Reynaud-Maurupt, 2012). In contrast, freebase enjoys a much more positive image (OFDT, 2018; 2013; Dujourdy et al, 2010; Freye, 2009; O'Rourke, 1991; Perry, 1980). Although it has not been possible to identify evidence in other countries, it is probable that similar misrepresentations of the reality also occur outside mainland France.

One of the consequences of the above is that there appears to be no specific data at all on the prevalence of freebase use anywhere in the world at present, since much of the recent literature and datasets refer to crack [FCP] or to MCPs. And even when papers and reports explicitly mention "cocaine freebase" it is often difficult to tell if they mean freebase as it is defined here or crack [FCP] (Jekel et al., 1994; Gold et al., 1985), or something else altogether (Romo-Avilés et al., 2015).

There is little doubt that crack [FCP] is more prevalent on global drug consumer markets than freebase, and it has recently been argued that preparing and smoking freebase is an outdated, arcane practice falling into disuse (TNI, 2019). Yet this may not be the case everywhere and for every category of users, and use of freebase may go unreported in some markets such as the United States (Reuter and Caulkins, 2004)[17] and Europe (EMCDDA and Europol, 2019, Pawlik and Mahler, 2011). In Europe, EMCDDA data indicate that out of an estimated total of about 73 000 people entering treatment for cocaine problems in 2017, 15%, or about 11 000 people, sought treatment for problems related to use of crack [FCP], which is typically smoked. However, smoking/inhaling was reported as a route of administration by a larger proportion of those entering treatment for cocaine problems that year: a sizeable 26% of the total, or about 19 000 users (EMCDDA, 2019b). This could suggest that about 11%, or 8 000 people, of all cocaine treatment entrants in Europe smoked or inhaled cocaine but did not use crack [FCP], opening the possibility that at least some of them used freebase, or perhaps, as in the case of the Paris users mentioned above, what they (mis)conceived as "freebase". At any rate, this suggests that the number of users of FCPs in Europe is underestimated, as it probably also is in other world regions. The obvious conclusion is that more precise monitoring of the cocaine market is needed.

Whatever the case, the literature analysed here suggests that it is helpful for the purpose of understanding the phenomenon to distinguish freebase and crack [FCP] because they are produced using different techniques and chemicals, albeit from the same starting material (TNI, 2019; De Souza, 2014; Neves, 2013; UNODC, 2013; Ribeiro, 2012; Freye, 2009; Bono, 2008; Gootenberg, 2008; Blickman, 2006; Colussi-Mas et al., 2003; EMCDDA, 2001; Castaño, 2000; WHO and UNICRI, 1995; WHO, 1994). The key difference is how the cocaine is recovered from the solution in which it has been reacted with a weak base, and not whether the weak base used is ammonia or sodium bicarbonate as it is sometimes thought (OFDT 2013; 2018). In the case of freebase, the drug is recovered by liquid-liquid extraction using an organic solvent, typically diethyl-ether, which also purifies it. In the case of crack [FCP], little or no purification is involved as the cocaine base is recovered manually from the solution. Extraction with an organic solvent will typically result in a purer end product than the other method, but because it involves a flammable solvent, it is much more dangerous (Freye, 2009; Bono, 2008; Colussi-Mas et al., 2003; WHO, 1994).

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17 In a paper about the US markets for heroin and cocaine, Reuter and Caulkins note that "cocaine base" appears "most commonly in the form of 'crack'" thereby suggesting that other forms such as freebase can also be found (Reuter and Caulkins, 2004).

Crack [FCP]

Making crack [FCP] is not a sophisticated process and requires no background in chemistry or specialised equipment. It is achievable by using chemical ingredients available in supermarkets and "do-it-yourself" stores and utensils present in any household, for instance spoons, pots and pans, together with a source of heat like a cigarette lighter or a stove. Unlike freebase, little physical risk is involved in "cooking" crack [FCP] (see below). The relative ease and safety of its manufacturing probably explains why crack [FCP] has become a commercial product sold by dealers on many drug markets in Europe, the Americas and elsewhere.

Crack [FCP] is prepared by dissolving cocaine hydrochloride in water, then mixing a weak base such as sodium bicarbonate ($NaHCO_3$) or ammonia (NH_3) in the solution. This is then boiled until all precipitated cocaine base melts into an oily layer, which occurs fairly rapidly. As the solution becomes colder, the cocaine base oil solidifies at the bottom of the recipient and is recovered with a tool, for instance the point of a knife. The water is discarded. The cocaine base can then be cut into smaller pieces if necessary and dried in a microwave oven or under lamps, or even with a cloth or a piece of kitchen roll in the case of small amounts.

Crack [FCP] made using this method will usually contain most if not all of the impurities, diluents and adulterants present in the starting material, albeit sometimes in lesser amounts (Colley and Casale, 2014; Gostič et al., 2009; Bono, 2008; Bean, 1993; Shannon, 1988; Siegel, 1982). Commercial crack [FCP] manufacturers (as opposed to user-manufacturers) may further dilute and/or adulterate cocaine hydrochloride before processing it into crack [FCP] (CICAD, 2019b). When more sodium bicarbonate or ammonia than necessary is used for the preparation, as is often the case in practice, residues of these substances will be present in the final product. While sodium bicarbonate is unlikely to cause injury when inhaled, ammonia is acutely toxic and will damage the lips, mouth, windpipe and lungs if it has not been thoroughly washed and dried off before the crack [FCP] is smoked. For this reason, many harm-reduction organisations advise users to prepare crack [FCP] with sodium bicarbonate and not with ammonia.

Freebase: brief historical overview

Cocaine freebase became a fashionable product among some groups of cocaine users in the United States starting in the 1970s, approximately at the same time as the smoking of MCPs began to be identified as a problem in Peru (Jeri, 1984), but about 10 years before the emergence of the "crack [FCP] epidemic" in the United States. Although the information sources reviewed here address freebase in the United States only, it is likely that the product was also known and used in other regions including Europe at that period.

In the 1970s and 1980s demand for cocaine increased dramatically in the United States (Gootenberg, 2008), and cocaine powder was often viewed as a "soft" if relatively expensive drug associated with wealth, success and the artistic milieu. Particularly in California, several books about cocaine were published at that time, some in expensive, "coffee-table" formats. Titles included *The Pleasures of Cocaine* (Gottlieb, 1976) and the *Cocaine Consumer Handbook* (Lee, 1976), and contents combined text with glossy photographs and Art Deco drawings. These publications purported to teach readers about cocaine, its nature and history and the various ways in which it could be used, including smoking through pipes. Some even gave advice for buying and dealing cocaine. Most also warned about possible "undesirable side-effects" of cocaine use, many of which were attributed to cutting agents. The books often included chapters on how to purify cocaine powders, that is, how to detect and eliminate cutting agents, notably by subjecting the product to simple chemical processes using ammonia and ether, for instance (Gottlieb, 1976).

As the interest in cocaine grew and more people starting experimenting with the drug, a subgroup of freebase users, essentially smokers, developed. At first, it seems that making freebase was primarily presented as a method allowing users to obtain a purer product than the one they had bought from their dealers. Indeed, freebase was most frequently "cooked" by those who would smoke it and only very rarely bought from third parties (Siegel, 1982).

In the late 1970s, books focusing exclusively on freebase were published, promoting its effects as highly pleasurable and listing several preparation methods (e.g., Anvil, 1979). Kits for the small-scale preparation of freebase were sold in drug paraphernalia shops or by mail order. These commercially available kits included basic equipment and small amounts of chemicals like sodium bicarbonate, ammonia, sodium hydroxide and ether. Five such kits and 5 freebase preparation methods (including one involving the preparation of what we now call crack [FCP]) were evaluated in a scientific study carried out by the University of Southern California in the early 1980s (Siegel, 1982).

Like cocaine, or perhaps even more so since it was reserved for discerning users of "pure" cocaine, freebase was surrounded by an aura of prestige and has been described as "the top-of-the-line model of the Cadillac of drugs" (Perry, 1980) and "the couture version of crack" (O'Rourke, 1991). Many American freebase users were apparently well-off individuals (Perry, 1980). However, accidents occurred due to the use of the highly flammable ether in freebase preparation, and some users reported to hospitals with serious burns. In a frequently mentioned episode, the American comedian and actor Richard Pryor suffered severe burns after accidentally igniting the rum he used instead of water in his water-pipe during a 3-day freebase-smoking session in his Los Angeles mansion in 1980.

By the early 1980s, it had become apparent that the smoking of freebase could also be a source of significant health problems, especially because freebase use was difficult to control and users described engaging in compulsive freebase smoking binge sessions that could last for days. Freebase smoking began to be viewed as a medical problem as more users were seeking help and some scientists launched into clinical studies (Anonymous, 1982; Perez-Reyes, 1982). In the late 1980s, most media and scientific attention became focused on another, cheaper product where cocaine is in freebase form, crack [FCP], particularly on its reported connections with poverty, social problems and crime (Goldstein et al., 1988), and freebase subsided into the background.

Freebase preparation and purity issues

Although the preparation of freebase is a little more complex and much riskier than that of crack [FCP], it too can be achieved without special chemistry skills, material or chemicals. Making freebase requires dissolving cocaine hydrochloride in water and adding a weak base (such as sodium bicarbonate or ammonia). Then liquid-liquid extraction is performed by adding diethyl-ether $(C_2H_5)_2O$, or another volatile organic solvent, to the solution and by stirring or shaking it. This causes the solution to separate into 2 layers with the ether layer on top. The ether layer is removed and transferred to another receptacle where it is evaporated. The aqueous bottom layer is discarded. After evaporation of the ether, solid crystals remain, looking like small rocks or lumps.

Because the freebase recovery process, i.e. extraction with a solvent, also is a purification process, preparing freebase will often result in a purer form of cocaine than in the cocaine hydrochloride powders used as starting material or in crack [FCP][18]. That said, as is the case with crack [FCP], how pure the cocaine freebase is at the end of the process depends largely on the purity of the cocaine hydrochloride used as starting material, and to some extent on the organic solvent used. Indeed, extraction with ether will cause all water-soluble substances to be captured in the aqueous bottom layer, including some of the impurities and common diluents (e.g. sugars such as mannitol, glucose, lactose, sorbitol, etc.) present in the starting material, as well as possible ammonia and sodium bicarbonate residue. But many adulterants frequently found in cocaine hydrochloride powders, including, PTHIT substances including levamisole, caffeine, diltiazem, hydroxyzine, phenacetin, benzocaine, lidocaine, procaine, etc. (see section on adulterants below), will be entirely or partially captured in base form in the ether layer, and after evaporation of the ether, they will be part of the rock-like solids together with cocaine freebase, and their vapours will be inhaled by users (Mallette et al., 2013; UNODC, 2012; Pawlik and Mahler, 2011; Freye, 2009; Gostič et al., 2009; Bono, 2008; Shannon, 1988; Siegel, 1982). As a result, freebase will rarely be pure cocaine but simply purer cocaine.

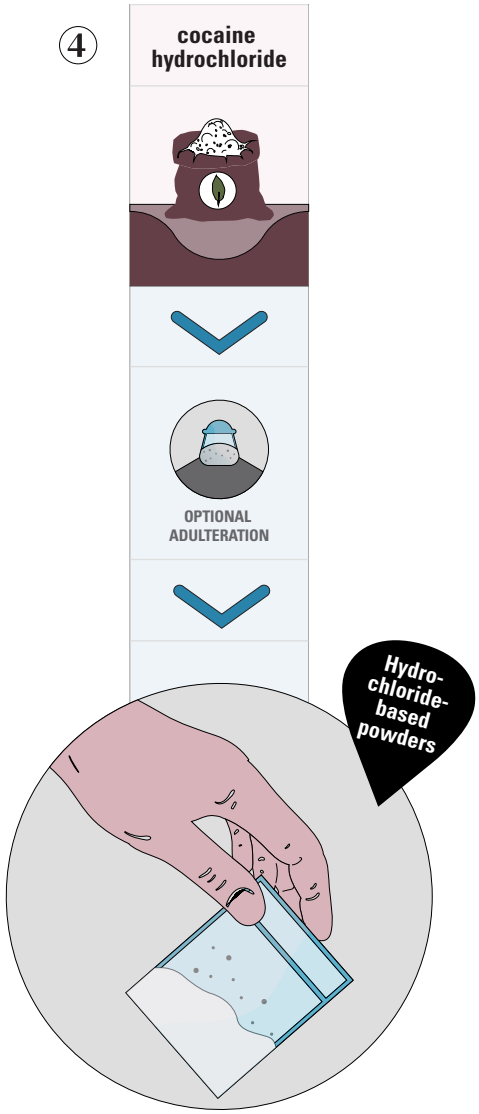
The dangers associated with this method are due to the use of an organic solvent, typically diethyl-ether, a highly flammable chemical that will ignite if subjected to heat or a flame. Thus, severe burns may result during the preparation of freebase, or when smoking it if it contains residual or larger amounts of ether (Freye, 2009; Bono, 2008; Siegel, 1982).

18 Liquid-liquid extraction with ether is one of the methods used to purify cocaine base made from coca paste (Casale and Klein, 1993; Schlesinger, 1985).

Bioavailability of cocaine through smoking of crack [FCP] and freebase

Although freebase and crack [FCP] will often be purer than the starting cocaine hydrochloride material, this does not necessarily mean that smoking will make cocaine bioavailable to the user, since a considerable proportion of the drug will frequently be trapped in the smoking device and in the respiratory tract of users and will not reach the lungs (and hence nor the bloodstream) (ElSohly et al., 1991; Perez-Reyes et al., 1982). For instance, it has been shown that smoking freebase or crack [FCP] in a tobacco or marijuana cigarette can result in a significantly lower bioavailability of the drug than smoking through a water-pipe (Siegel, 1982). In addition, the presence of adulterants can drastically decrease the amount of cocaine actually entering the lungs. A study has shown that cocaine base vapours decompose in the presence of paracetamol, reducing the amount of cocaine inhaled by the user. The proportion of the cocaine that remains available to produce effects depends on how much paracetamol is present. In a mixture consisting of equal parts of cocaine base and paracetamol about 97% of the cocaine is reported to be destroyed; in a mixture containing just 10% of paracetamol some 70% of the cocaine is reported destroyed (Gostič et al., 2009).

Cocaine hydrochloride: a mixed bag of unpredictable powders



Powder is what comes to people's minds when they think of cocaine and powder is how cocaine hydrochloride is most frequently made available to consumers on illicit global markets, according to the information available. There is very little specific information on non-powder forms of cocaine hydrochloride, such as solids, or on powdered cocaine base (Dujourdy et al., 2010), and both appear to be considerably rarer than cocaine hydrochloride powders. As a result, and although it is reported to be practically impossible to visually distinguish powders containing cocaine hydrochloride from those containing cocaine base (Dujourdy et al., 2010), use of the term "powder cocaine" has become widespread as a practical, though imprecise (King, 1997), way of distinguishing consumer products containing cocaine hydrochloride from those containing cocaine base and especially "crack cocaine" (or crack [FCP] as it is called in this report) (CICAD, 2019a; DEA, 2019; EMCDDA, 2019b; 2018a; UNODC, 2019b; Fischer et al., 2016; NIDA, 2016; Shearer et al. 2005). This section is based on the information that is available and therefore it focuses exclusively on cocaine powders and, unless specified, assumes that all contain cocaine hydrochloride.

Strictly speaking, the powders sold as cocaine to consumers around the world are practically never 100% pure cocaine hydrochloride. In other words, all powders will contain substances other than cocaine hydrochloride in greater or lesser amounts (while some "fakes" will have no cocaine at all). Cocaine hydrochloride powders are therefore best understood as mixtures of a range of different substances present in varying, unpredictable proportions.

Two categories of non-cocaine hydrochloride substances are most commonly reported in the cocaine powders seized around the world: impurities and cutting agents. These substances come from 3 different sources: the plant material used to manufacture cocaine hydrochloride; the cocaine manufacturing process; and the process of dilution and adulteration implemented by markets actors, i.e. cocaine producers and traffickers (Schlesinger, 1985). Cutting agents account for by far the largest proportion of the non-cocaine material usually found in most cocaine hydrochloride powders.

Impurities

It should be noted that, in contrast to cutting agents, some impurities will practically always be present in the cocaine hydrochloride products made available to global consumers (Casale and Klein, 1993; Soine, 1986)[19]. This is very likely to include products that are sometimes reported to contain "only cocaine" or even "pure cocaine" by drug-checking services, which infrequently test cocaine samples for impurities and rarely report on diluents (McDonald et al., 2020; Payer et al., 2020; Brunt et al., 2016; Caudevilla et al., 2016; Ventura et al., 2011; TEDI, n.d.).

Alkaloids

One of the families of impurities found in cocaine hydrochloride consumer products arise from the plant material. They consist in several natural compounds, that is, the alkaloids present in coca leaves that have not, or not totally, been eliminated during the cocaine manufacturing process, for instance by oxidation with potassium permanganate. Different species, varieties, and cultigens of the coca plant will yield different ranges of alkaloidal impurities in cocaine hydrochloride powders. Additional alkaloidal impurities may be generated by the manufacturing process itself through the chemical modification of cocaine and other coca alkaloids. A third type of alkaloidal impurities may emerge from the degradation of cocaine hydrochloride, cocaine base and coca paste due to heat and humidity such as may occur when these products are stored for a long period and/or in poor conditions. Analysis of alkaloids present in cocaine samples can be useful for determining the varieties of coca plants used for cocaine manufacturing as well as some aspects of the manufacturing process, for instance the extent of oxidation of the cocaine or the types of solvent used.

Cis-cinnamoylcocaine, trans-cinnamoylcocaine and tropacocaine appear to be the alkaloids present in larger amounts in most illicit cocaine hydrochloride powders (Zacca et al., 2014; Comunidad Andina, 2013; Casale et al., 2008b; By et al., 1988; Soine, 1986). Other commonly found alkaloidal impurities include benzoylecgonine, ecgonine, methylecgonine (ecgonine methyl ester), hydroxycocaines, norcocaine, trimethoxycocaine, truxillines and others. Concentrations of alkaloidal impurities in cocaine hydrochloride samples are reported to range from tiny amounts to a not negligible 10% of the total (Cui et al., 2019; Mallette et al. 2018; Maldaner et al., 2016; Monfreda et al., 2015; Stride Nielsen et al., 2016; Botelho et al. 2014; Casale et al., 2014; Mallette and Casale, 2014; Zacca et al., 2014; Comunidad Andina, 2013; Casale et al., 2007; Fucci, 2007; Moore and Casale, 1994; Casale and Klein, 1993; Gómez and Rodríguez, 1989; Soine, 1986; Schlesinger, 1985).

Solvents and other chemicals

The preparation of cocaine hydrochloride from coca leaf will be an additional source of some of the non-cocaine material found in products sold to the end consumer. Although a series of other residues including acids and bases are also found in consumer cocaine powders (Magalhães et al., 2013), solvents are the most frequently reported residues of illicit cocaine manufacturing. Most solvents are highly toxic substances, and even if they are usually present in residual amounts in cocaine powders, repeated exposure in frequent users may lead to a series of negative health outcomes (Garzón et al. 2009).

Solvents are used at several stages of the manufacturing process and small amounts are almost always occluded in the crystals of illicit cocaine hydrochloride powders sold to consumers. Solvents encountered in cocaine hydrochloride products may also have been added after the manufacturing process, for instance as impurities in cutting agents (Morello and Meyers, 1995). A wide range of residual solvents have been found in cocaine hydrochloride samples over the years since different solvents are used in different combinations at different times by illicit cocaine manufacturers in Bolivia, Colombia and Peru. For example, a study of 65 samples taken from several 1-kilo bricks of cocaine hydrochloride seized in Colombia identified a total of 28 different solvents (Garzón et al. 2009).

A wide variety of solvents were also detected in cocaine hydrochloride samples analysed in Europe and in the United States since the early 2000s. For example, a forensic study in Denmark in the mid-2010s identified the presence of a total of 13 different solvents in just 5 samples of seized cocaine hydrochloride, while individual samples each contained between 4 and 9 different solvents (Stride Nielsen et al., 2016). Fifteen years earlier an Italian study had identified a total of 32 different solvents in 47 samples of cocaine hydrochloride (Chiarotti et al., 2002).

Solvent combinations change over time as illicit manufacturing processes evolve constantly in response to changes in manufacturing methods, to new opportunities for procuring specific solvents and to precursor control and enforcement measures implemented in cocaine producing countries and in source countries for cocaine chemicals. A recent example of such shifts is an increase in the use of acetate solvents other than ethyl acetate when converting cocaine base to cocaine hydrochloride (INCB, 2020; 2019).

Solvents commonly found in cocaine hydrochloride consumer products include acetone, benzene, chloroform, diethyl-ether, ethanol, ethyl acetate, hexane, isobutanol, isopropylacetate, methylene chloride, metyl etyl ketone (MEK), n-propyl acetate, toluene, etc. (Stride Nielsen et al., 2017; 2016; Monfreda et al., 2015; Colley and Casale, 2014; Dujourdy et al., 2010; Dujourdy and Besacier, 2008; Casale et al., 2008a; Chiarotti et al., 2002; Schlesinger, 1985).

19 Casale and Klein (1993) note that even pharmaceutical cocaine is not 100% pure.

Forensic analysis of changes in the solvent profiles of cocaine hydrochloride samples can also be useful in order to identify changes in illicit cocaine manufacturing methods. A recent illustration is the identification of a trend in which illicit cocaine manufacturers now process multi-kilogram batches of cocaine base into cocaine hydrochloride, whereas in the past cocaine hydrochloride was produced 1 kilogram at a time (Mallette et al. 2018).

Cocaine base alongside cocaine hydrochloride

In addition to the impurities commonly found in cocaine powders, some powders also appear to contain cocaine base alongside cocaine hydrochloride. The presence of cocaine base in cocaine powders is reported to be unintended and due to incomplete, i.e. faulty, crystallization of cocaine base into cocaine hydrochloride in the illicit manufacture process. The analysis of about 12,500 samples of cocaine powders seized in France has shown that powders containing both cocaine base and cocaine hydrochloride were seized every year over a 20-year period (1990-2009). In some years, such mixtures represented almost 20% of all cocaine powders seized and analysed in the country (Dujourdy et al., 2010; Dujourdy and Besacier, 2008). Similar base-hydrochloride mixtures were found in Brazil (Zacca et al., 2014), and in a small number of samples of cocaine seized in Canada in 2019 (CSP, 2020).

Although sources describing similar situations in other countries have not been found, it is likely that powders containing mixtures of cocaine base and cocaine hydrochloride exist on global consumer markets on a larger scale than the available data suggest. This information gap could be due, at least partly, to the fact that specific tests (e.g. infra-red spectrometry) required to confirm the presence of cocaine hydrochloride in samples are not always performed in forensic laboratories (King, 1997).

Cutting agents: diluents and adulterants

It is well-known that cutting agents, also known as additives, cheaper than cocaine are commonly added to cocaine hydrochloride powders by market actors along the illicit distribution chain mainly in order to increase profits by increasing product volume. However, some cutting agents are likely to serve additional purposes as well (see below). Unlike precursors and essential chemicals, cutting agents are typically not subject to international control, although some may be subject to controls under national legislation, including health and/or food legislation.

An obvious prerequisite for a substance to be used as a cutting agent in cocaine powders is that it must physically resemble the substance sought by buyers so that they do not become aware of the fact that they are obtaining a diluted or adulterated product. Therefore, most cocaine cutting agents are white or off-white powders.

Some cutting agents, specifically adulterants, are added at the last stage (crystallization) of the cocaine hydrochloride manufacturing process at buyers' request; buyers are reported to supply the adulterants and to specify the amounts to be added to the cocaine hydrochloride (SIMCI, 2019b; INCB, 2018; 2017). However, cocaine is also frequently cut at all subsequent stages (Morelato et al., 2019; Broséus et al., 2016; Magalhães et al., 2013; Caulkins and Reuter, 1998). As a result, cocaine hydrochloride consumer products are likely to be among the powder drugs most subject to dilution and adulteration, at least in the Americas and Europe (CICAD, 2019a; Broséus et al., 2016; Karch and Drummer, 2015; TEDI, n.d.). For instance, there is evidence suggesting that cocaine hydrochloride powders are more heavily and more frequently diluted than heroin powders in Europe. Wider varieties of diluents and adulterants were found in larger amounts and in more samples of cocaine hydrochloride consumer products than in heroin products in comparative or comparable studies involving thousands or hundreds of cocaine hydrochloride samples (Morelato et al., 2019; Broséus et al., 2015b; 2016; Schneider and Meys, 2011; Dujourdy and Besacier, 2010; Dujourdy et al., 2010; Andreasen et al., 2009).

Two categories of cutting agents may be distinguished: diluents and adulterants. Diluents are inert, pharmacologically inactive substances. Many diluents found in cocaine products are routinely used in the food industry (e.g. sugars, starches, bicarbonates), and like the other products used to dilute cocaine, they can be purchased with relative ease and at comparatively low prices.

Adulterants are pharmacologically active substances, and they tend to be more expensive and harder to procure since they may be subject to more national controls, as many of them are pharmaceutical drugs. Importantly, several of the adulterants frequently found in cocaine products are harmful substances that amplify the toxicologic effects of cocaine. In fact, some adulterants may be more harmful than cocaine itself (Knuth et al., 2018; Brunt et al., 2017; Hammond and Craven 2017; Martelo et al., 2017; Solomon and Hayes, 2017; Busardò et al., 2016; CICAD, 2016a; Indorato et al., 2016; Pawlik et al. 2015; Barbera et al., 2013; Comunidad Andina, 2013; Pilgrim et al., 2013; Kachiu et al., 2012; Karch et al., 2012; Larocque and Hoffman, 2012; Buchanan et al., 2010; Cole et al., 2010; Knowles et al., 2009; Raymon, and Isenschmid, 2009; Fucci, 2004; Karch, 1996; Shesser et al., 1991; Curini et al., 1989; Shannon, 1988).

Diluents

Diluents, sometimes called bulking agents, fillers or excipients, are pharmacologically inert substances whose only function, other than inconspicuously bulking up cocaine products, can be aesthetic, that is, giving powders an aspect and consistency that will be appealing to consumers. Less information about diluents is available in the scientific literature than about adulterants, which may be due to the fact that most diluents are viewed as posing less health risks to cocaine consumers than do many adulterants (Solomon and Hayes, 2017). However, high concentrations of diluents in cocaine products can lead to negative health outcomes (TEDI, n.d.), for instance maize starch and talc when cocaine is injected (Shannon, 1988).

A wide variety of diluents have been found in samples of cocaine hydrochloride consumer products. The evidence indicates that dilution of cocaine hydrochloride occurs in producing, transit and consumer countries, but perhaps more so in the latter two (Morelato et al., 2019; Sant'Ana et al. 2019; SIMCI, 2019b; Zacca et al., 2014; Magalhães et al., 2013; Cunningham et al., 2010; Shannon, 1988). Diluents found in cocaine hydrochloride samples in Brazil, Canada, Chile, Europe, Morocco and the United States since the mid-1980s include sugars (dextrose, fructose, glucose, inositol, lactose, sucrose, maltose, mannitol, sorbitol, etc.) and other substances such as ascorbic, boric, citric and tartaric acids, carbonates and bicarbonates (e.g. calcium carbonate), sodium chloride (table salt), potato, wheat and maize starches, sulphates (e.g. aluminium sulphate, plaster), talc and other silicates, etc. (Duffau et al., 2020; CICAD, 2019b; Morelato et al., 2019; Sant'Ana et al., 2019; Da Silva, 2018; Solimini et al., 2017; Stambouli and El Bouri, 2017; Maldaner et al, 2016; Broséus et al., 2015b; Monfreda et al., 2015; Duffau et al., 2014 ; Magalhães et al., 2013; Neves, 2013; Brunt, 2012; Cole et al., 2011; Cole et al., 2010; Dujourdy et al., 2010; Andreasen et al., 2009; Neves and Nunes, 2008; UNODC, 2005 ; Gonçalves de Carvalho and Mídio, 2003; Fucci and De Giovanni, 1998; King, 1997; Curini et al., 1989; Gómez and Rodríguez, 1989; Shannon, 1988; Janzen, 2013; Cunningham et al., 1984; Siegel, 1982).

Trends in use of diluents are difficult to identify due to variations in both the diluents used by market actors in different settings at different times and the methodologies and scopes (periods covered and sample numbers) of the relatively few recent studies from which diluent information can be retrieved. That said, the literature reviewed here tentatively suggests that between the 1980s and the mid-2010s the cocaine diluents most frequently found in South America were carbonates and bicarbonates (Duffau, 2020; Sant'Ana et al., 2019; Duffau et al., 2014; Magalhães et al., 2013; Bernardo et al., 2003; Gonçalves de Carvalho and Mídio, 2003; Morales-Vaca, 1984), whereas those most frequently used in Europe were sugars (Morelato et al., 2019; Broséus et al.,

2015a; Cole et al., 2011; Dujourdy et al., 2010; Andreasen et al., 2009; Brunt et al., 2009; Decorte, 2001; Fucci, and De Giovanni, 1998; King, 1997; Gómez and Rodríguez, 1989; BBC, n.d.).

Adulterants

Adulterants added to cocaine hydrochloride powders consist of a wide range of pharmacologically active substances that most frequently includes medicines, more rarely other illicit drugs like amphetamine and methamphetamine (Payer et al., 2020; Kudlacek et al., 2017; Cole et al., 2011; Brunt at al., 2009; Gómez and Rodríguez, 1989), and even more rarely new psychoactive substances (Payer et al., 2020; Kudlacek et al., 2017; Vidal et al., 2014). Adulterants are usually costlier and may be more difficult to procure than diluents, and as a result they have long been suspected to serve purposes other than simply bulking up cocaine products (Shannon, 1988).

A specific "grey" market for adulterants found in cocaine and other drug products exists in Europe (EMCDDA and Europol, 2016; ACMD, 2015; Broséus et al., 2015b; 2016; Dujourdy and Besacier, 2010) and probably in other regions such as the Americas.

Adulterants account for the largest proportion of the non-cocaine hydrochloride material most frequently reported in cocaine consumer products, and they can pose significant additional health risks because of their individual properties and their interactions with cocaine or with one another (Pawlik et al., 2015). Yet their presence in cocaine products is not routinely monitored using standardized chemical analysis methodologies at international or regional level (CICAD, 2019b; Lociciro et al., 2008), although, according to the INCB (2019), this would be possible under article 13 of the United Nations Convention against Illicit Traffic in Narcotic Drugs and Psychotropic Substances of 1988. One of the consequences is that this gap renders comparisons across regions or countries, and over time, of the prevalent cutting practices of market actors—for the purposes of strategic analysis and public health interventions—both more difficult to implement and less reliable (Broséus, et al., 2016; Busardò et al., 2016; Barrio et al., 1997).

As is the case with diluents, the adulterant content of hydrochloride powders varies widely in terms of the number of individual substances used, their different combinations, and their concentration relative to cocaine. Adulterant contents also change with time (Broséus, 2016), and the range of adulterants found in cocaine hydrochloride samples has increased since the 1980s in Europe and the Americas, when mostly local anaesthetics were used, and especially since the early- to mid-2000s (CICAD, 2019b; Broséus et al., 2015a; 2015b; Brunt, 2012; Cole et al., 2010; Brunt et al., 2009; Casale et al., 2008b). However, there are indications that adulterant concentrations in cocaine powders have decreased recently in several European markets and in the United States, where cocaine purity has increased (DEA, 2019; EMCDDA and Europol, 2019; Verri et al., 2019; Gómez and Rodríguez, 1989; Shannon, 1988).

The wide range and diversity of adulterants used to cut cocaine products illustrates the complexity and dynamism of the phenomenon of cocaine adulteration and of the global cocaine market in general. Thus, a UNODC (2005) manual for forensic laboratories has listed 30 substances (including five controlled drugs) as frequently encountered adulterants in cocaine products, whereas 38 (including two controlled drugs) were listed in a paper published in the United States in the early 1990s (Shesser et al. 1991), and a report states that 50 different adulterants were found in consumer cocaine powders seized in the United Kingdom in the mid-2010s (ACMD, 2015). Nonetheless, according to the literature reviewed for this report, the number of different adulterants of cocaine hydrochloride consumer products identified in individual studies reporting chemical analysis results published over the past 30 years or so varies roughly between 5 and 15 different substances.

Over the past 15 years, the most frequently encountered adulterants in cocaine hydrochloride products have been caffeine, diltiazem, hydroxyzine, levamisole and dexamisole, paracetamol and phenacetin as well as a range of local anaesthetics led by lidocaine (sometimes called lignocaine) but also including benzocaine, prilocaine, procaine and tetracaine. The information available suggests that local anaesthetics are the substances with the longest history of use as cocaine adulterants, while levamisole (a substance widely used in veterinary medicine) and phenacetin (an analgesic) appear as those most frequently found in the last 10 to 15 years (Duffau et al., 2020; INCB, 2020; Payer et al., 2020; CICAD, 2019b; Cui et al., 2019; Fiorentin et al., 2019; INCB, 2019; SIMCI, 2019b; Bertol et al., 2018; Da Silva et al., 2018; INCB, 2018; Villar, 2018; Brunt et al., 2017; INCB, 2017; Stambouli and El Bouri, 2017; De Souza et al., 2016; Maldaner, 2016; Marcelo et al., 2015; Broséus et al., 2015a; 2015b; Lapachinske et al., 2015; Botelho et al., 2014; Eiden et al., 2014; Floriani et al., 2014; Comunidad Andina, 2013; Casale et al., 2012; Schneider and Meys, 2011; Ventura et al., 2011; Cole et al., 2010; Dujourdy et al., 2010; Evrad et al., 2010; Andreasen et al., 2009; Brunt et al., 2009; Maietti et al., 2009; Behrman et al., 2008; McGill et al., 2008; Neves and Nunes, 2008; Kenyon et al., 2005; Fucci and De Giovanni, 1998; Barrio et al., 1997; King, 1997; Gómez and Rodríguez, 1989; Shannon, 1988; Cunningham et al., 1984; Siegel, 1982; Anvil, 1979; Lee, 1976; BBC, n.d.; TEDI, n.d.).

Most of the adulterants found in cocaine hydrochloride powders are pharmaceutical drugs, although in some cases their use in human medicine has been discontinued or restricted in many countries due to their adverse effects (e.g. levamisole, phenacetin). The main adulterants of cocaine belong to the following pharmacologic or therapeutic families, with some belonging to more than one family: local anaesthetics, analgesics (pain killers),

Data and information sources about adulteration of cocaine powders used in this report

A fairly large body of information about adulterants in cocaine hydrochloride consumer products available in several drug markets does exist in the literature, but most published studies cannot be said to be representative of national situations and they often cover different time periods. The few relatively recent studies reporting results of analysis of thousands of samples seized over long periods of time that could be viewed as a better reflection of national or subnational situations and trends, are necessarily limited to the timeframe and locations they cover and they usually only take place once (Villar et al., 2018; Broséus et al., 2015b; Comunidad Andina, 2013; Dujourdy et al., 2010; Brunt et al., 2009). Another limiting factor is that the vast majority of the information found in published forensic reports relates to illicit markets in Brazil, Canada, several, mostly western, European countries and the United States. These and other limitations combine to make the evidence, and the image that can be built from the literature, generally patchy, even in the comparatively few markets where evidence is available.

The majority of the publicly available information on adulterants present in cocaine hydrochloride consumer products reviewed in this report comes from two sources:

- Official forensic laboratories of national or sub-national authorities reporting results of chemical analysis of seized samples, which make up the majority of the literature reviewed here; and
- Drug checking services reporting information on analysis performed on cocaine hydrochloride products submitted to them by users.

A limitation affecting most forensic studies comes from their source material, that is, samples of cocaine products seized by law enforcement authorities, which often include cocaine exchanged between market actors as well as consumer products, and are therefore not always focused neatly on the latter. That said, the adulterants identified in seizures of larger amounts of cocaine are more than likely to also be found further down the chain, at consumer level. Another limitation of many of these studies is their lack of immediacy, that is, they tend to be reflections of past states of affairs and often feature results of analysis of samples that were seized several years before publication.

A useful source in this respect is the regular analysis of seizure samples, such as in the United States by the Cocaine Signature Program, which has reported data for several years on concentrations of phenyltetrahydroimidazothiazole (PTHIT), i.e. levamisole, its stereoisomer dexamisole, and combinations thereof, in samples of wholesale cocaine seizures carried out in the United States market (Mallette et al., 2013; Casale et al. 2012; Casale et al., 2008b; Valentino and Fuentecilla, 2005).

Publicly available reports of drug checking services can also provide useful specific information on adulterants encountered in cocaine consumer products. In addition, they tend to be more timely than forensic studies, often reflecting present or very recent situations. However, they are rarely representative of national or even subnational situations. Another limitation is that most such services exist only in Canada, eight European countries and the United States, and they are primarily active in nightlife settings (Maghsoudi et al., 2020; McDonald, 2020; Payer et al., 2020; EMCDDA, 2018b; Brunt, 2017; Ventura et al., 2011; DrugsData, n.d.), thereby underrepresenting or excluding other contexts in which cocaine is used.

Some insight into adulterants in cocaine hydrochloride consumer products can also be gained from studies analysing residue in syringes used to inject drugs. However, injection appears to be much less frequently used than other routes of administration for cocaine, while syringe residue analysis is a relatively novel technique and there have been few reports from a handful of European cities so far (EMCDDA, 2019a; Néfau et al., 2015).

Data on adulterants from drug checking and syringe residue analysis have been added recently to the range of sources regularly used in the monitoring of the drug market in the European Union (EMCDDA, 2019a; 2019b) and similar initiatives also exist in Canada (Maghsoudi et al., 2020; Payer et al. 2020). In future, this may help improve knowledge about cocaine hydrochloride consumer products available on some markets.

anthelminthic (anti-worm), antihistamines (anti-allergy), antipyretics (fever reducing), anxiolytics, sedatives, stimulants (sometimes called "nootropics") and vasodilators (heart medication). Many cocaine adulterants pose significant health risks, some of which are summarised in Table 1 (CICAD, 2019b; Knuth et al., 2018; Brunt et al., 2017; Hammond and Craven 2017; Martelo et al., 2017; Busardò et al., 2016; Indorato et al., 2016; Broséus et al., 2015a; Pawlik et al. 2015; Barbera et al., 2013; Comunidad Andina, 2013; Pilgrim et al., 2013; Brunt, 2012 ; Larocque and Hoffman, 2012; Karch et al., 2012; Cole et al., 2011; Ventura et al., 2011; Buchanan et al., 2010; Cole et al., 2010; Fucci, 2004; Karch, 1996; Shannon, 1988).

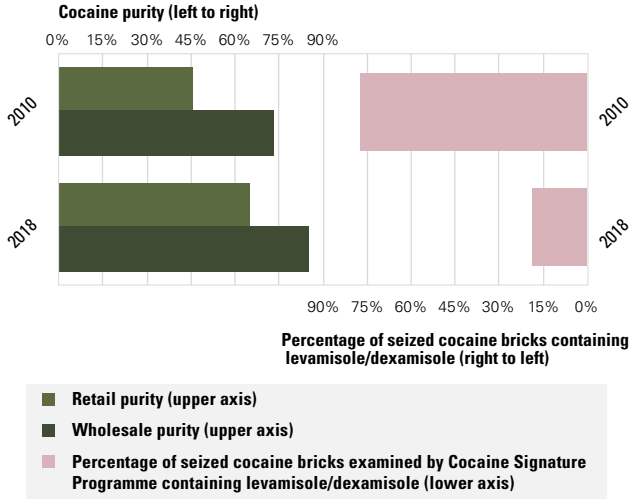
However, it must be stressed that the properties for which these substances are or were used to treat patients may not necessarily be those that are sought by the market actors who add them to cocaine products. Which properties do market actors seek then? According to the literature reviewed here, for some adulterants their motivations seem transparent but in several other cases, including harmful substances, there are no certainties. In addition, although the toxicity of specific cocaine adulterants is generally known when they are used as medicines, often as tablets administered orally, this may not be the case when they are used in combination with cocaine or other adulterants and/or via different routes of administration such as nasal insufflation and smoking (Pawlik et al., 2015; Brunt et al., 2009). Thus, the issue of cocaine adulteration and its effects on health remains a partial knowledge gap.

Purity of cocaine hydrochloride products and changes in the global market

Although it is also a reflection of the efficiency of illicit manufacturing facilities, cocaine purity appears almost as an image in negative of dilution and adulteration, as illustrated in Figure 3: the more cutting agents are mixed into cocaine products, the less pure they are, and vice-versa.

Another aspect is worth noting: the impact of cocaine adulteration at the source. Considering that levamisole is known to be added primarily to Colombian cocaine crystallization laboratories (SIMCI, 2019b), Figure 3 also appears to indicate that, at least since 2010, adulteration at the source has had a major impact on wholesale purity and, more surprisingly, on retail purity of cocaine hydrochloride products in a major destination market, that of the United States. Indeed, it is often reported that dilution and adulteration occur primarily *after* cocaine has left production facilities and especially at levels closer to the retail market (Morelato et al., 2019; Broséus et. al, 2016; Cunningham et al., 2010; Kilmer and Hoorens, 2010; Caulkins and Reuter, 1998). While Figure 3 does not necessarily disprove this, it may reflect an increased availability of cocaine in the global cocaine market in the 2010s.

FIG. 3 Cocaine purity versus adulteration with levamisole/dexamisole, United States, 2010 and 2018



Sources:
Purity: Office of National Drug Control Policy
Adulteration:
- 2010: DEA cocaine signature programme, data summarized in: Casale, J., Colley, V. and LeGatt, D. (2012), "Determination of Phenyltetrahydroimidazothiazole Enantiomers (Levamisole/Dexamisole) in Illicit Cocaine Seizures and in the Urine of Cocaine Abusers via Chiral Capillary Gas Chromatography–Flame-Ionization Detection: Clinical and Forensic Perspectives", Journal of Analytical Toxicology, vol. 36, n°2, March.
- 2018: Drug Enforcement Administration. January 2019 CSP Report, DEA PRB 05-13-19-09, 2019.

Other products

Although this appears to be rare, it is worth mentioning that cocaine-containing products made to look like medicines can occasionally be encountered on illicit markets. The United States Drug Enforcement Administration (DEA) recently reported that tablets and capsules containing cocaine are sporadically seized in the United States. In the 2018-2019 period, some of the capsules seized contained cocaine only, but in other instances cocaine was found in tablets also containing other controlled substances such as buprenorphine and alprazolam (Xanax). For instance, in Massachusetts in January 2019, cocaine was found in combination with alprazolam in a counterfeit prescription 2-milligram alprazolam tablet while similar tablets seized at the same time were found to contain alprazolam combined with fentanyl. The DEA does not specify the amounts of cocaine found in each tablet/capsule or if the drug was in base or hydrochloride form (DEA, 2019). As far as is known, tablets or capsules containing cocaine have not been reported anywhere else in the world in recent years.

It is difficult to ascertain how these products were destined to be used based on the information reported by the DEA. However, it can be doubted that they were meant to be ingested orally since this route of administration would result in the destruction of 60% to 70% of the cocaine before it had produced any effect.

The use of levamisole as an adulterant

Levamisole has been described as "the ideal cutting agent" (Solomon and Hayes, 2017) and it is certainly the cocaine adulterant on which most information is available. This is undoubtedly due to its toxicity and near ubiquitous presence in cocaine samples tested around the world in the last 15 years, although most of the literature on levamisole relates to cocaine markets in Europe and North America. However, it should be noted that other substances such as caffeine and phenacetin have been used to adulterate cocaine products for a longer period of time than levamisole and have often been found in higher concentrations and in more samples than levamisole (SIMCI, 2019b; Comunidad Andina, 2013; Dujourdy et al., 2010; Brunt et al., 2009; Gómez and Rodríguez, 1989).

Levamisole, an isomer of phenyltetrahydroimidazothiazole (PTHIT), was originally developed as an anthelmintic medicine for humans and animals in the mid-1960s (Solomon and Hayes, 2017). Use of the drug in human medicine was subsequently abandoned due to severe adverse effects. At present, levamisole is widely used in many countries as a veterinary medicine in order to get rid of worms in caprine, bovine, ovine and porcine livestock. Although levamisole is generally no longer used in human medicine, it still has a very restricted number of applications in some countries, for instance as a kidney drug for children, as an adjuvant in treatment of colon cancer or in treatment of rheumatoid arthritis (Brunt et al., 2017; CICAD, 2016a; ANSM, 2014; Kachiu et al., 2012). It is worth noting that residues of levamisole and other anthelmintic drugs used to treat livestock have been identified in varying concentrations in cooked beef and pork meats and their juices, and are therefore also likely to be ingested by the non-cocaine-using, meat-eating population (Cooper et al., 2011).

Levamisole is added to cocaine hydrochloride powders by producers in South America, essentially in Colombia (SIMCI, 2019b; INCB, 2018; 2017; Comunidad Andina, 2013; Casale et al., 2012; Garzón et al. 2009; Casale et al. 2008b) but some may also be added in other producing, transit or consumer countries. It is possible that, initially, levamisole was added to cocaine hydrochloride mainly in products destined to be exported out of South America, possibly in mixtures containing other adulterants.

Soon after it was detected as an ingredient in cocaine hydrochloride powders for the first time in the United States in 2003 (Casale et al., 2008b; Valentino and Fuentecilla, 2005), levamisole-adulterated cocaine hydrochloride was also identified in Canada in 2004 (LeGatt et al., 2007) and in Europe. It was detected for the first time in France and in the Netherlands in 2004 (Dujourdy et al, 2010; Brunt et al., 2009), in Luxembourg in 2006 (Schneider and Meys, 2011), "significantly detected" for the first time in Switzerland in 2006 (Broséus et al., 2015b), and first reported in Italy in 2007 (Fucci, 2007). In Morocco, it was detected for the first time in 2009 (Stambouli and El Bouri, 2017).

In mid-2010, illicit cocaine manufacturers also started adding tetramisole, alone or in combination with levamisole, as an adulterant in cocaine. Tetramisole is a commercially available anthelmintic made up of equal proportions of levamisole and dexamisole, the other isomer of phenyltetrahydroimidazothiazole (PTHIT) (Casale et al., 2012).

By the end of the 2000s and up to the mid-to-late-2010s, it is likely that levamisole, alone or in combination with tetramisole, was present in many, then most, cocaine hydrochloride powders sold in Australia (Pope et al., 2018), Europe and North America. Starting in April 2009 it was detected in more than 50% of the 1-kilo cocaine bricks seized in the United States and analysed by the DEA's Cocaine Signature Program (CSP) (Casale et al., 2012). The same year, about 45% of the cocaine hydrochloride products seized and analysed in France contained levamisole (Dujourdy et al., 2010) and levamisole became the main adulterant in cocaine seized in Switzerland (Broséus et al., 2015b), while it was found in 48% of cocaine hydrochloride samples tested in Spain by Energy Control, a harm reduction organisation (Ventura et al., 2011). By 2015, the DEA determined that 93% of 730 analysed samples from cocaine bricks seized in the United States contained levamisole or PTHIT mixtures (CSP, 2016), while in the Netherlands, about 70% of the more than 1 300 consumer cocaine hydrochloride powders tested by the Trimbos Institute contained levamisole (Trimbos Instituut, 2016). It is also worth noting that levamisole was detected in 63% of 154 cocaine hydrochloride samples seized in Morocco between 2007 and 2016, making it by far the most frequently found cutting agent in the study (Stambouli and El Bouri, 2017).

In South America, however, levamisole appears to have been detected in cocaine products, particularly consumer products, later than in North America and Europe, although not enough data is available to make any definite judgements. Thus, in Chile a tiny 0.07% of 8 800 mostly consumer cocaine hydrochloride samples analysed in 2009 contained levamisole, and a little more than 4% of 5 500 samples in 2013 (Duffau et al., 2015). In Brazil, none of the 513 cocaine hydrochloride samples seized in the south-eastern state of Espirito Santo over 2008-2012 were reported to contain levamisole, and neither were samples seized by the Federal Police during roughly the same period,

although in both cases it is unclear if the methodologies used sought to identify levamisole specifically (De Souza et al., 2016; Zacca et al. 2014).

Nevertheless, levamisole was found in seizures of larger amounts of cocaine in Brazil, or in cocaine destined to be shipped out of Brazil, in the late-2000s to early 2010s. The adulterant was detected in about 8% of 1 085 cocaine samples taken from seizures of wholesale amounts carried out in seven Brazilian states between 2009 and 2013 (Grobério et al., 2015). Levamisole was also found in 19% of 210 samples seized throughout Brazil between 2009 and 2012 (Botelho et al., 2014), and in more than 55% of samples of cocaine departing Brazil seized at the international airport of Sao Paulo and in mailing services in 2011 (Lapachinske et al., 2015). In Colombia, a little less than 8% of 65 samples from domestically produced 1-kilo cocaine hydrochloride bricks were reported to contain levamisole in 2009 (Garzón et al., 2009).

Interestingly, in the European countries for which enough data is available, initial detection of levamisole appears to have occurred in coincidence or close sequence with detection of hydroxyzine and diltiazem in cocaine hydrochloride, and there are indications that it is also the case in the United States (McGill et al., 2008). In the Netherlands, levamisole, diltiazem and hydroxyzine were all detected for the first time in 2004 (Brunt et al. 2009); in Italy, levamisole and hydroxyzine were detected in the same year (Fucci, 2007); and in France, hydroxyzine was first detected in 2003 and diltiazem and levamisole in 2004 (Dujourdy et al., 2010). In subsequent years, the presence of all 3 cutting agents was detected in cocaine hydrochloride samples in every year covered by Dutch, French, Luxembourgish and Swiss studies (Broséus et al., 2015b; Schneider and Meys, 2011; Dujourdy et al, 2010; Brunt et al., 2009).

In addition, a standardized chemical analysis of hundreds of samples of cocaine base and hydrochloride consumer products seized in 2012 in Bolivia, Colombia and Peru indicates that Colombia was the only country where levamisole, diltiazem and hydroxyzine were found as adulterants. The same report concluded that levamisole was the substance most frequently used as an adulterant in cocaine hydrochloride bricks exported to large consumer markets (Comunidad Andina, 2013).

All this suggests that, starting around the early-to-mid-2000s, mixtures containing diltiazem, hydroxyzine and levamisole in different concentrations were added in Colombia to some cocaine hydrochloride products destined to be exported to Europe and North America at the request of the owners of the cocaine and in quantities specified by them (SIMCI, 2019b; INCB, 2018; 2017; Comunidad Andina, 2013; Casale et al., 2012; Casale et al., 2008b). Initially, such traffickers may have been illicit actors involved in the exportation and wholesale of cocaine products to the European and North American markets, while buyers acting on South American markets did not request adulterants. Later on, in the early-to-mid-2010s, cocaine adulterated with levamisole, diltiazem and hydroxyzine also appeared in products sold to Colombian users (Comunidad Andina, 2013), and to users elsewhere in South America (CICAD, 2019b), including Brazil (Ribeiro de Araújo et al., 2019) and Chile (Duffau et al., 2020).

Some recent data suggest that use of levamisole (and other adulterants) as an additive in cocaine products started to decrease in the mid-to-late 2010s, at least in the United States and in Europe (no recent data is available for the rest of the world). In 2017, for the first time since 2009, less than 50% of the cocaine bricks seized in the United States and analysed by the DEA contained levamisole (CSP, 2018). The proportion of levamisole-containing bricks tested by the DEA has further declined since, with the latest report indicating that 16% of analysed bricks seized in the United States during the first half of 2020 contained the substance (CSP, 2021). In Europe, the Dutch Information Monitoring System (DIMS) reports a continuous decrease in the proportion of thousands of consumer cocaine hydrochloride products containing levamisole it tested between 2015 (74%) and 2018 (35%) (Trimbos Instituut, 2019). The EMCDDA and Europol (2019) also report a decrease in cocaine adulteration in Europe, and under 20% of 830 cocaine samples tested by drug checking organisations in 7 countries in the first half of 2018 contained levamisole (EMCDDA, 2019b).

TABLE 1 Six adulterants frequently found in cocaine powders

Adulterant	Levamisole (and other PTHIT)	Phenacetin	Diltiazem	Hydroxyzine	Lidocaine (and similar substances)	Caffeine
Main properties and licit uses	**Anthelmintic (animals), immuno-modulator**, widely used in livestock (bovine, ovine, porcine), no longer used in humans due to severe adverse effects, except in very few instances (see box on levamisole).	**Analgesic, antipyretic**, no longer used in medicine in many countries due to adverse effects.	**Calcium channel blocker, vasodilator,** widely used in heart medications.	**Antihistamine,** used as anxiolytic, sedative and antiemetic.	**Local anaesthetic,** widely used in dentistry and for nasal anaesthesia.	**Stimulant,** widely used in cold medicines and energy drinks.
Possible reasons and motivations for presence alongside cocaine (other than bulking)	Wide availability as a veterinary medicine (20), inexpensive to buy and twice heavier than cocaine for the same volume (19); adds a sheen to repackaged cocaine bricks, enabling further adulteration of cocaine products down the trafficking chain (19); may potentiate or prolong the pleasurable effects of cocaine (13, 14, 15), probably due to the action of its metabolite aminorex (12, 21) (see below); some users report that they prefer cocaine hydrochloride products containing levamisole to those not containing levamisole (30).	Availability as an analgesic medicine in some South American countries and elsewhere (6, 15); bitter taste similar to cocaine; enhances aspect of cocaine by adding a shine to powders (3, 15); slight euphoric effect when used with caffeine; may help minimize side effects of cocaine or another adulterant (17).	Once alleged to minimize cardiovascular toxicity of cocaine, but this has been proven false; may reduce side effects of cocaine (17); gives a false positive for cocaine on some colorimetric tests (16), which may help dissimulate the extent of cocaine adulteration.	Has local anaesthetic effects (23) (see reasons for use of lidocaine and similar substances); long-acting sedative effect may give users the impression that they will be able to sleep even after using cocaine (17).	Disguises loss of cocaine potency due to addition of cutting agents (1); mimics numbing effects of cocaine on nose and mouth (1, 3); nasal anaesthetic effect may facilitate use of large doses of cocaine (3); gives a false positive for cocaine on some colorimetric tests (16), which may help dissimulate the extent of cocaine adulteration.	Bitter taste similar to cocaine (23, 24); similar stimulating, yet milder, properties as cocaine (1, 24); may enhance felt effects of cocaine (23).
Harmful effects associated with prolonged use or use in high doses	Exact physiologic effects when used with cocaine are not clear; levamisole affects white blood cells; prolonged use is potentially lethal; may enhance toxic effect of cocaine on cardiovascular system (17); has led to cases of severe agranulocytosis, neutropenia, arthralgia, pulmonary hypertension, retiform purpura, skin necrosis, leukoencephalopathy (4, 7, 8, 9, 10, 18, 19, 24, 27); less severe adverse effects include nausea, vomiting, headache, fatigue, fever, diarrhoea, myalgia, dizziness, confusion, and rash (24).	Toxicity on kidneys, blood and cardiovascular system, and suspected carcinogenicity (1, 3, 15); toxicity on liver when combined with alcohol (15).	Potentiates toxicity of cocaine; may lead to cardiovascular issues including angina, hypotension and arrhythmia (5, 17).	Rare adverse effects include dizziness (6) and convulsions (15); may potentiate toxic effects of cocaine (17).	Can potentiate toxic effects of cocaine including cardiac arrhythmia, convulsions and seizures (3); high dose can lead to hallucinations and seizures (22); may cause pulmonary injury (17). Benzocaine in large doses can lead to methaemoglobinaemia, a blood condition (6).	Moderate to high doses can lead to serious harm including death (2); may potentiate toxic effects of cocaine (3); chronic use may incur withdrawal symptoms (6).
Notable seizures	Bolivia reported seizing 100 kg in 2016 (28).	Bolivia reported seizing about 580 kg in 2016 (28).				Brazil reported seizing more than 2 tons in 2015 (28).
Also note	Some levamisole may be manufactured illegally in South America (26). Levamisole metabolises in the body into aminorex, an amphetamine-like substance used in the past as an appetite suppressant in some European countries (24); aminorex is suspected to have been used to dope racing horses in North America, Western Europe and China (27). Rare instances of illicit manufacture of aminorex for sale as a drug have been detected (25). Aminorex has stimulating effects that are distinct and much more potent than those of levamisole, and that are comparable to those of cocaine (24); due to the longer duration of its effects compared to cocaine, it is thought to prolong the effects felt by cocaine users (21, 24); aminorex is known to cause hypertension but this effect has yet to be connected to use of cocaine products (10, 21); levamisole can be used to adulterate heroin in Colombia (29).	One of the metabolites of phenacetin is acetaminophen (paracetamol), which is also frequently used as an adulterant in cocaine (and heroin) products.				Caffeine is likely to be the substance most widely used to adulterate illicit drug products at global level. In addition to cocaine, it is also frequently found in heroin, ecstasy/MDMA, amphetamine and methamphetamine products.

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CRIMJUST

Going Beyond Drug Seizures

CRIMJUST is implemented by UNODC in partnership with INTERPOL and Transparency International. CRIMJUST seeks to enhance law enforcement and judicial strategies beyond interdiction activities and to foster transnational responses along drug trafficking routes targeting each stage of the drug supply chain. This includes the production of knowledge on the cocaine market to support evidence-based policy and strategies designed to counter the cocaine threat.

GIFP

Global Illicit Flows Programme

Funded by the European Union